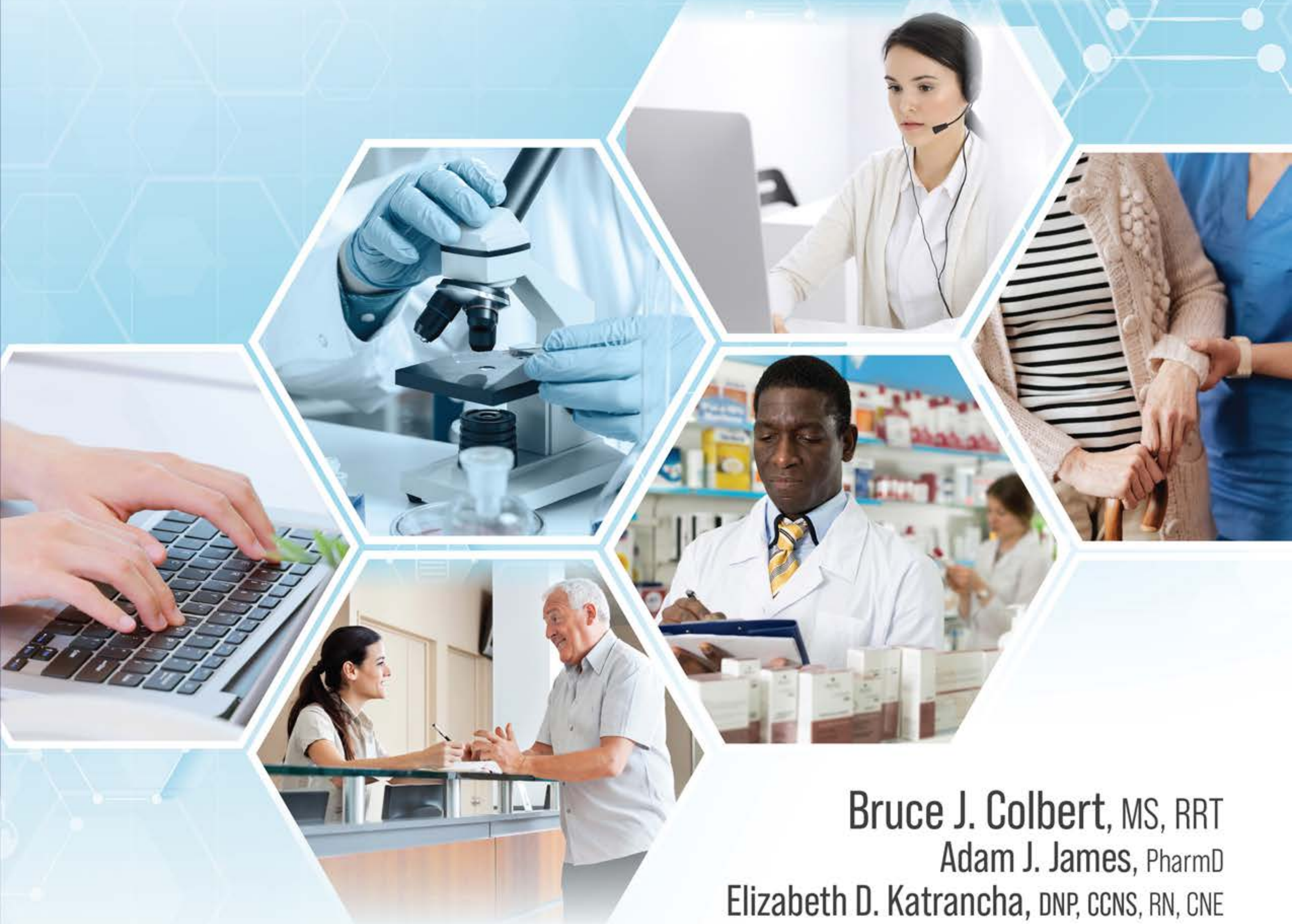
Cengage

10th Edition

Essentials of Pharmacology

for Health Professions



Bruce J. Colbert, MS, RRT
Adam J. James, PharmD
Elizabeth D. Katrancha, DNP, CCNS, RN, CNE

10th Edition

Essentials of Pharmacology for Health Professions

Bruce J. Colbert, MS, RRT
Past Director of Allied Health
Programs
Clinical Associate Professor Emeritus
University of Pittsburgh at Johnstown
Johnstown, Pennsylvania

Adam J. James, PharmD
Rite Aid Pharmacy Clinical Team/
Duquesne University of Pharmacy
Manager for Immunization and Clinical
Programs for Rite Aid Pharmacy
Johnstown, Pennsylvania

Elizabeth D. Katrancha, DNP, CCNS, RN, CNE
Veteran's Health Administration
Johnstown, Pennsylvania

Всё для победы!
НАРОДНЫЙ ФРОНТ
https://pobeda.onf.ru/
LET'S HELP THE RUSSIA

Cengage

Australia • Brazil • Canada • Mexico • Singapore • United Kingdom • United States

Cengage

***Essentials of Pharmacology for Health Professions,* Tenth Edition**
Bruce J. Colbert, Adam J. James,
Elizabeth D. Katrancha

SVP, Product Management: Cheryl Costantini

VP, Product Management: Mark Santee

Portfolio Product Director: Laura Stewart

Portfolio Product Manager: Andrea Henderson

Product Assistant: Renee Bunszel

Learning Designer: Debra Myette-Flis

Course Lead: Ken McGrath

Content Project Manager: Dinesh Deivendiran

Manager, Product Marketing: Annie Gillingham

Content Acquisition Analyst: Erin McCullough

Production Service: MPS Limited

Designer: Felicia Bennett

Cover Image Source: michaeljung/Shutterstock.com; Gravity Images/The Image Bank/Getty Images; Paola Giannoni/E+/Getty Images; Iakov Filimonov/Shutterstock.com; U.P.SD/Shutterstock.com; Dmytro Zinkevych/Shutterstock.com; Iryna Rahalskaya/Shutterstock.com; BearFotos/Shutterstock.com; Alex_Traksel/Shutterstock.com; Tyler Olson/Shutterstock.com; iStock.com/iStock Signature

Copyright © 2026 Cengage Learning, Inc. ALL RIGHTS RESERVED.

WCN: 02-300-527

No part of this work covered by the copyright herein may be reproduced or distributed in any form or by any means, except as permitted by U.S. copyright law, without the prior written permission of the copyright owner.

Previous edition(s): © 2023, © 2019, © 2015

For product information and technology assistance, contact us at
Cengage Customer & Sales Support, 1-800-354-9706
or support.cengage.com.

For permission to use material from this text or product, submit all requests online at **www.copyright.com**.

Library of Congress Control Number: 2024926877

ISBN: 979-8-214-11606-8

Cengage
5191 Natorp Boulevard
Mason, OH 45040
USA

Cengage is a leading provider of customized learning solutions. Our employees reside in nearly 40 different countries and serve digital learners in 165 countries around the world. Find your local representative at: **www.cengage.com.**

To learn more about Cengage platforms and services, register or access your online learning solution, or purchase materials for your course, visit **www.cengage.com.**

Всё для победы!
НАРОДНЫЙ
ФРОНТ
https://pobeda.onf.ru/
LET'S HELP THE RUSSIA

Printed in the United States of America
Print Number: 01 Print Year: 2025

Contents

List of Tables / vii
Dedication / ix
Preface / xi

Part 1 Introduction to Pharmacologic Principles

Chapter 1
Consumer Safety and Drug Regulations 2
Drug History / 3
Pharmacology Timeline / 4
Drug Laws / 5
FDA and DEA / 10
Health Care Professionals and the Law and Ethics / 10

Chapter 2
Drug Names and References 15
Classifications / 16
Identifying Names / 17
Legal Terms Referring to Drugs / 20
Terms Indicating Drug Actions / 21
Drug References / 23
The Internet as Reference / 23

Chapter 3
Sources and Bodily Effects of Drugs 26
Sources of Drugs / 27
Effects of Drugs / 29
Drug Processing by the Body (Pharmacokinetics) / 29
Other Variables Affecting Drug Action / 33
Unexpected Responses to Drugs / 39

Chapter 4
Medication Preparations and Supplies 44
Drug Forms and Devices / 45
Supplies / 57

Chapter 5
Abbreviations and Systems of Measurement 63
Abbreviations / 63
Systems of Measurement / 69

Chapter 6
Safe Dosage Calculations 77
Calculation Guidelines / 82
Method 1: Basic Calculation / 83
Method 2: Ratio and Proportion / 86
Pediatric Dosage / 89
Geriatric Dosage / 91
Prevention of Medication Errors / 91

Chapter 7
Responsibilities and Principles of Drug Administration 97
Responsible Drug Administration / 97
Medication Errors / 99

Principles of Administration / 100
MedWatch / 104

Chapter 8
Administration by the Gastrointestinal Route 109
Administration of Medications Orally / 111
Administration of Medications Rectally / 116
Administration of Rectal Suppository / 117
Administration of Medications by Percutaneous Endoscopic Gastrostomy (PEG) or Nasogastric Tube (NGT) / 118

Chapter 9
Administration by Parenteral and Other Routes 124
Sublingual and Buccal Administration / 125
Transcutaneous Drug Delivery System / 126
Inhalation Route / 128
Injections / 131
IV Medications / 145
Skin Medications / 146
Eye Medications / 146
Ear Medications / 148

Chapter 10
Poison Control 157
Poisoning by Ingestion / 158
Poisoning by Inhalation / 159
External Poisoning of Skin or Eyes / 160
Poisoning by Sting and Snakebite / 160
People at Risk / 161

Part 2 Drug Classifications

Chapter 11
Nutritional Concepts of Pharmacology 168
Fat-Soluble Vitamins / 170
Water-Soluble Vitamins / 174
Minerals / 183
Antioxidants / 192
Alternative Medicines / 193
Suggested Readings / 200

Chapter 12
Integumentary System Medications 203
Antipruritics / 204
Corticosteroids / 205
Emollients and Protectants / 206
Keratolytics / 207
Enzyme Preparations / 207
Scabicides and Pediculicides / 209
Local Anti-Infectives / 211
Burn Medications / 217
Agents Used to Treat Acne / 219
Topical Immunomodulators / 220
Cautions for Topical Medications / 221

Chapter 13
Autonomic Nervous System Drugs 225
Adrenergics / 228
Adrenergic Blockers / 231
Cholinergics / 233
Cholinergic Blockers / 235

Chapter 14
Cardiovascular System Medications 240
Cardiac Glycosides (Digoxin) / 241
Antiarrhythmic Agents / 243
Antihypertensives / 250
Other Antihypertensives / 253
Coronary Vasodilators / 257
Antilipemic Agents / 260
Antithrombotic Agents / 266
Thrombolytic Agents / 272
Hematopoietic Agents / 273

Chapter 15

Urinary System Drugs 279
Diuretics / 279
Medications for Gout / 285
Bladder Antispasmodics / 289
Cholinergics / 291
Urinary Analgesics / 292
Treatment of Benign Prostatic Hyperplasia / 294

Chapter 16

Gastrointestinal Drugs 300
Antacids / 301
Agents for Treatment of Ulcers and Gerd / 302
Gastric Mucosal Agents / 304
GI Antispasmodics or Anticholinergics / 307
Agents for Inflammatory Bowel Disease / 308
Antidiarrheal Drugs / 310
Antiflatulents / 313
Laxatives and Cathartics / 315
Antiemetics / 321

Chapter 17

Respiratory System Drugs and Antihistamines 328
Respiratory Diseases and Disorders / 328
Oxygen Therapy / 329
Respiratory Stimulants / 329
Bronchodilators / 330
Corticosteroids / 336
Asthma Prophylaxis / 338
Mucolytics and Expectorants / 340
Antitussives / 342
Antihistamines / 344
Decongestants / 347
Safety of Cough–Cold–Allergy Products / 349
Smoking-Cessation Aids / 350

Chapter 18

Eye and Ear Medications 358
Anti-Infectives / 358
Anti-inflammatory Agents / 360
Antiglaucoma Agents / 363
Mydriatics / 370
Local Anesthetics / 371
Otic (Ear) Medications / 372

Chapter 19

Central Nervous System Drugs: Analgesics, Sedatives, and Hypnotics 378
Analgesics / 378
Antimigraine Agents / 392
Sedatives and Hypnotics / 395

Chapter 20

Psychotropic Medications, Alcohol, Drug Abuse, and Withdrawal Treatment 403
CNS Stimulants / 404
Selective Norepinephrine Reuptake Inhibitor (SNRI) for ADHD / 407
Antidepressants / 409
Antimanic Agents / 416
Anxiolytics / 418
Antipsychotic Medications/Major Tranquilizers / 422
Substance Abuse / 429
Alcohol / 429
Alcohol Poisoning / 431
Prescription Drug Abuse / 432
Illegal Drug Abuse / 433

Chapter 21

Musculoskeletal and Anti-Inflammatory Drugs 441
Skeletal Muscle Relaxants / 441
Anti-Inflammatory Drugs / 444
Osteoporosis Therapy / 449

Chapter 22

Anticonvulsants, Antiparkinsonian Drugs, and Agents for Alzheimer’s Disease 457
Anticonvulsants / 458
Drug Therapy for Generalized and Partial Seizures / 460
Drug Therapy for Febrile Seizures / 462
Drug Therapy for Absence Seizures / 462
Antiparkinsonian Drugs / 465
Agents for Restless Legs Syndrome / 472
Agents for Alzheimer’s Disease / 472

Chapter 23
Endocrine System Drugs 478

Pituitary Hormones / 479
Adrenal Corticosteroids / 480
Thyroid Disorders / 483
Antidiabetic Agents / 488

Chapter 24
Reproductive System Drugs 507

Gonadotropics / 507
Androgens / 508
Erectile Dysfunction Medications / 510
Estrogens / 512
Progestins / 515
Choice of Contraceptives / 520
Drugs for Labor and Delivery / 524
Other Gonadotropic Drugs / 529

Chapter 25
Anti-Infective Drugs 534

Resistance / 535
Adverse Reactions / 536
Immunizations / 537
Monoclonal Antibody Vaccines / 538
Antibiotics / 538
Aminoglycosides / 540
Cephalosporins / 541
Macrolides / 542
Penicillins / 544
Carbapenems / 545
Quinolones / 547
Tetracyclines / 549
Antifungals / 550
Antituberculosis Agents / 552
Miscellaneous Anti-Infectives / 556
Agents for VRE / 557
Sulfonamides / 560
Urinary Anti-Infectives / 561
Antivirals / 562
Treatment of Human Immunodeficiency Virus/AIDS Infections / 565

Chapter 26
Antineoplastic Drugs 573

Antimetabolites / 576
Alkylating Agents / 577
Mitotic Inhibitors / 577
Antitumor Antibiotics / 580
Hormones and Hormone Modifiers / 580
Biological Therapies / 581
Colony-Stimulating Factors (CSFs) / 582
Monoclonal Antibodies (MABs) / 582
Targeted Therapies / 583
Vaccines / 584
Radioactive Isotopes / 585
Cautions and Responsibilities for Antineoplastic Drugs / 585

Chapter 27
Age-Related Medication Issues 592

Older Adult Considerations / 593
Physiologic Changes with Increasing Age / 593
Potentially Inappropriate Medication Use in Older Adults / 596
Drugs to Avoid with Certain Medical Conditions / 596
Polypharmacy / 599
Issues with Adherence / 601
Pediatric Considerations / 602

Summary / 609
Comprehensive Exam for Part 1 / 611
Comprehensive Exam for Part 2/ 617
Glossary / 623
Index / 639

List of Tables

1-1 Five Schedules of Controlled Substances
2-1 Common Drug Classifications and Examples
2-2 Comparison of Drug Names
2-3 Examples of Combination Drugs
3-1 Processing of Drugs within the Body
3-2 Examples of Pharmacogenomic Laboratory Tests
4-1 Common Abbreviations for Drug Administration
5-1 Common Abbreviations for Medication Orders
5-2 Metric Equivalents for Solid (Grams) and Liquid (Liters) Measurement
5-3 Meaning of Metric System Prefixes
5-4 Common *Approximate* Equivalents for Liquid Measurement
9-1 Types of IV Fluids
11-1 Summary of Fat-Soluble and Water-Soluble Vitamins
11-2 Ranges for Select Electrolytes in the Body
11-3 Summary of Major Minerals
11-4 Herbs
12-1 Topical Medications for the Skin: Antipruritics, Emollients and Protectants, Keratolytics, and Enzymatics
12-2 Medications for the Skin: Scabicides, Pediculicides, Antifungals, Antivirals, Antibacterials, and Antiseptics
12-3 Medications for the Skin: Burn Medications, Acne Medications, and Topical Immunomodulators
13-1 Adrenergic Receptors
13-2 Representative Adrenergic Medications
13-3 Representative Alpha- and Beta-Adrenergic Blockers
13-4 Representative Cholinergic Medications
13-5 Representative Cholinergic Blockers
14-1 Cardiac Glycosides and Antiarrhythmics
14-2 Antihypertensives
14-3 Coronary Vasodilators
14-4 Antilipemic Agents
14-5 Anticoagulants
14-6 Platelet Inhibitors, Thrombolytic Agents, and Hematopoetic Agents
15-1 Drugs for Diuresis
15-2 Antigout Medications
15-3 Bladder Antispasmodics
15-4 Agents for BPH
16-1 Antacids, Antiulcer Agents, and Gastric Mucosal Agents
16-2 GI Antispasmodic, IBD, Antidiarrheal, and Antiflatulent Agents
16-3 Laxatives
16-4 Antiemetics
17-1 Bronchodilators
17-2 Corticosteroids
17-3 Asthma Prophylaxis Agents

17-4 Mucolytics and Expectorants
17-5 Antitussives
17-6 Antihistamines and Decongestants
17-7 Smoking-Cessation Aids
18-1 Anti-inflammatory Ophthalmic Drugs
18-2 Antiglaucoma Agents
18-3 Mydriatics and Local Anesthetics for the Eye
18-4 Otic Preparations and Medications for Earwax Build-up
19-1 Opioid Analgesics[a]
19-2 Nonopioid Analgesics and Antipyretics, Local Anesthetics, Medical Marijuana and cannabinoids
19-3 Adjuvant Analgesics
19-4 Antimigraine Agents
19-5 Sedatives and Hypnotics (Use Hypnotics Short-Term Only)
20-1 Central Nervous System Stimulants and Nonstimulant Medications
20-2 Antidepressants
20-3 Antimanic Agents
20-4 Antianxiety Medications (Anxiolytics)
20-5 Antipsychotic Medications/Major Tranquilizers
21-1 Skeletal Muscle Relaxants
21-2 Nonsteroidal Anti-Inflammatory Drugs
21-3 Agents for Osteoporosis Prevention and Therapy
22-1 Anticonvulsants
22-2 Antiparkinsonian Drugs
22-3 Agents for Alzheimer's Disease (AD)
23-1 Pituitary and Adrenal Corticosteroid Drugs
23-2 Thyroid and Antithyroid Agents
23-3 Diabetes Type I vs. Type II
23-4 Insulins
23-5 Oral and InjecTable Noninsulin Antidiabetic Agents
24-1 Androgen Agents
24-2 Erectile Dysfunction (ED) Agents
24-3 Estrogens and Progestins
24-4 Contraceptive Agents
24-5 Drugs for Labor and Delivery
24-6 Other Gonadotropin-Associated Drugs
25-1 Anti-Infective Agents: Aminoglycosides, Cephalosporins, Macrolides, Penicillins, and Carbapenems
25-2 Anti-Infective Agents: Quinolones, Tetracyclines, Antifungals, and Antituberculosis Agents
25-3 Miscellaneous Anti-Infectives and Agents for VRE
25-4 Sulfonamides and Urinary Anti-Infectives
25-5 Antivirals
25-6 Drugs for HIV/AIDS
26-1 Antineoplastic Agents
26-2 Side Effects of Antineoplastic Agents

Dedication

In Memorial

To my loving wife Patty, whose love, zestful spirit, and especially smile inspired my life and work. She was the loving mother of two great kids, Joshua and Jeremy, and her wonderful daughter-in-law Ali. While Bubba only had a little time with her granddaughter Lenyx, she left a spirit impression that will be with her all her life and is now watching over her and her new brother Luxton. Heaven has indeed gained a very bright light!

Bruce Colbert

To Ruth Woodrow, the original author of this textbook whose passion for education and providing a meaningful learning experience for her students was ever foremost in both her mind and heart. We spoke often about the need to keep the material simple, relevant, and meaningful for the students. I remember a dedication she wrote to her grandchildren Ashston, Jeff, Samantha, and Eric that said, "may you realize that knowledge is power and seek to learn all your lives." She was a sweet gentle soul who is missed by her family and dear husband Roger.

Bruce Colbert

Ruth Woodrow spoke often of her belief in lifelong learning. Throughout her life, she helped others on their learning journey through her teaching, tutoring, volunteering, and sharing of knowledge. Ruth would often break into teaching moments during our conversations as she pointed out connections between the content, real-world illnesses, and the drugs used to treat them. I felt privileged to engage in a private "lesson" on pharmacology as Ruth guided me to the section of content that I should read to learn more. Her commitment and dedication to making learning pharmacology accessible to everyone by focusing on what students need to know continues to guide the text.

Debra Myette-Flis, Learning Designer, Cengage

Message to the Students

When I first started teaching over 40 years ago it quickly became clear that many of my students had a fear of pharmacology, which they thought was the most difficult course in our program. I set out to change that mindset and while it took a few years for me to figure out the solutions, it was well worth it.

I found that many students were relying solely on mass memorization and this became overwhelming given the type and amount of material. I worked to change their method to truly "learning" the material, and this led to not only short-term success in the course but long-term success in their professions. So, what are some main strategies to truly learn? One of the first is to take difficult material and relate it to something you know and understand. In Chapter 13 on the autonomic nervous system, for example, we use a snarling dog to show the sympathetic responses instead of simply listing them. Now you "know" that when the sympathetic nervous system is stimulated, your pupils dilate to get more light in to see the situation, and your heart rate and breathing (along with bronchodilation) increase to get more vital oxygen to your muscles to ready you for fight or flight. Now you know this forever thanks to a relatable story.

Some other methods that foster true learning are:

- Study in groups and select areas to teach each other (you really learn something when you have to teach it).
- Make up stories and use visualization to relate material. For example, visualize a congested highway opening up another lane to relieve the pressure, which relates to vasodilators used to treat hypertension.
- You probably have family members on some of the medications and if appropriate discuss with them, especially how it makes a difference in their lives.

I hope the way the text is written in a friendly style along with the engaging electronic assets helps you truly "learn" the material, which will carry you through this class and on to your professional career.

Bruce Colbert

Preface

Goals of This Book

The main purpose of this text is to serve as an engaging and relevant source for students studying nursing, medical assisting, and various allied health fields such as health information management, surgical technology, and respiratory care. In addition, it can serve as an excellent resource for continuing education updates for professionals in health care.

The goal of this text is to provide an extensive framework of knowledge that can be acquired within a limited amount of time. A varied and engaging series of electronic experiences is available to complement the text to bring the material to life for today's students.

This text will be especially helpful for learners in 1-year training programs with limited time allotted to the study of medications. This text has been specially designed to meet the needs of learners in nursing and medical assistant programs. However, learners in all health care programs will find the concise format adaptable to their needs.

This text has been field tested in several classes with learners in various health professions. Learners who have already used this text for updating or supplemental education include registered nurses, licensed practical nurses, medical assistants, surgical technologists, respiratory therapists, and pharmacy technicians.

Those employed in health professions now have increased responsibilities for providing the necessary information to their patients regarding the safe administration of medications, side effects, and interactions. Patient education is presented in every chapter in Part II. Even if you are not directly involved in patient education, it is imperative you understand what information is being conveyed.

Organization and Features of the Text

The quantity of information could be overwhelming and confusing to the learner unless presented in a reader-friendly manner.

The text's comprehensive yet concise format reduces the massive quantity of information and unnecessary detail that may tend to overwhelm or confuse the learner. Outdated or rarely used medications, obsolete information, and complex descriptions are eliminated. The information is both factual and functional.

The text is broken down into two specific parts. ***Part I*** can stand alone as a basic but comprehensive review of pharmacologic principles. ***Part I*** introduces the learner to the fascinating subject of drugs, their sources, legal concerns, and their medical uses. *Review questions* at the end of each chapter help the learner assess their understanding of the chapter material. Medication preparation, supplies, and specific information on each route of administration are covered. *Administration checklists* allow the learner to put the knowledge into practice. Upon the completion of Part I the learner will have all the foundational knowledge to study and understand the specific drug classifications in Part II.

Part II organizes the drugs according to classifications, arranged in logical order. Each classification is described, along with the characteristics of typical drugs, their purposes, side effects, cautions or contraindications, and interactions. Please note cautions and contraindications are combined as one category since it is clear from the explanation where the drug *is not to be used* in a certain situation (contraindication) and where it *can be used* in a certain situation but should be monitored closely (cautions). A special icon ❗ identifies the most common or most important side effects of drugs. This special icon is meant to serve as a valuable guide for learners. Rather than memorizing every side effect for each drug, the icon emphasizes the side effects with which health care professionals should be most familiar. *Patient education boxes* for each category are highlighted. These special boxes will assist health care professionals to educate patients and answer their questions about the medications they are taking.

Easy-to-use *reference tables* with each classification list the most commonly prescribed drugs according to their generic and trade names, with dosage and available forms.

Reality-based case studies in each chapter in Part II present drug usage scenarios in a variety of settings and stimulate critical thinking by providing practical application of drug information.

Chapter *review quizzes* assist learners to identify areas for further study. *Comprehensive review quizzes* for Part I and Part II encourage learners to practice for the final test.

An extensive *glossary* lists and defines key terms used in the text and defines non-key terms that might not be common knowledge such as unusual side effects. A comprehensive index includes both generic and trade names.

New to This Edition

Before discussing what has changed in this edition, it is important to note what hasn't changed. We have dedicated the revision to enhancing the user-friendly writing style with more analogies and learning hints to keep the style that has made this pharmacology text popular.

Global Text Changes

- Each drug classification has been updated with the latest and most frequently prescribed drugs available.
- Tables have been added and updated to give concise and practical information.
- Patient education boxes have been expanded.
- Clinical Connection features have been added to give a real-life application to the material being discussed to enhance its relevancy.
- Several new illustrations and photos have been added to provide learners with a visual connection to the material.
- All relevant websites have been updated.
- Review questions have been updated and new questions have been added to cover new material.
- The glossary has been expanded to include new terms beyond just the key terms.

Some specific changes include the following:

- Simplified drug dosage calculations to include a basic but very relevant math review
- Expanded clinical application boxes show the relevancy of learning the material
- More information on pediatric pharmacology
- The latest on COVID-19 treatments and vaccines
- Newer drug treatments for weight
- Information on topical immunomodulators
- Biologics used for treatment of gout
- Up-to-date pain treatment strategies to lower opioid use
- Updated immunization information and schedules

Instructor and Student Resources

Additional instructor and student resources for this product are available online. Instructor assets include an Instructor's Manual, Educator Guide, PowerPoint® slides, Solution and Answer Guides for answers to the chapter review quizzes, Part 1 and 2 comprehensive review exams, and case studies in the text, Comprehensive Drug Worksheets with answers, and a test bank powered by Cognero®. Student assets include PowerPoint® slides including images and a focus on the key concepts from each chapter.

The Instructor Manual includes the following:

- Additional review quizzes with answers
- An alternate Comprehensive Exam for Part II with answers

Sign up or sign in at **www.cengage.com** to search for and access this product and its online resources.

MindTap

MindTap is a fully online, interactive learning experience built upon authoritative Cengage Learning content. By combining readings, multimedia, activities, and assessments into a singular learning path, MindTap elevates learning by providing real-world application to better engage students. Instructors customize the learning path by selecting Cengage Learning resources and adding their own content via apps that integrate into the MindTap framework seamlessly with many learning management systems.

The guided learning path demonstrates the relevance of basic pharmacology principles to health care professions through engagement activities, interactive exercises, and procedural videos. The Pronounce activity ensures correct pronunciation of the most commonly prescribed 200 drugs, plus additional hospital drugs. Easy-to-use *reference tables* with each classification list the most commonly prescribed drugs according to their generic and trade names, with dosage and available forms, special considerations, and audio to encourage correct pronunciation of the drugs most likely to be encountered in health care. Learners apply an understanding of pharmacology through application-based media quizzes. These media quizzes elevate the study of pharmacology by challenging students to apply concepts to practice.

To learn more, visit www.cengage.com/training/mindtap.

About the Authors

Bruce Colbert is a retired Associate Professor and Director of the Allied Health Care Department at the University of Pittsburgh at Johnstown, Pennsylvania, where he achieved faculty emeritus status. The author of 12 traditional books, he also developed an interactive worktext and DVD program on student success. Focusing on such topics as stress and time management, he has presented more than 250 regional and national lectures and workshops devoted to professional skills, enhancing critical and creative thinking, and effective decision making. In addition, Mr. Colbert consults with educational programs to improve teaching effectiveness as well as presents active teaching workshops.

Adam James is the Manager for Immunization and Clinical Programs for Rite Aid Pharmacy, focusing on immunization planning, implementation, and organization for almost 2,500 Rite Aid locations. He is the co-author of two textbooks, as well as a contributor to educational materials for Cengage. He continues to be a preceptor for Duquesne University School of Pharmacy, and he was awarded Duquesne University Preceptor of the Year in 2020. In addition, Dr. James is a published CPE author, certified through ACPE.

Elizabeth Katrancha is a former Associate Professor and Program Coordinator of the Baccalaureate Nursing Program at the University of Pittsburgh at Johnstown, Pennsylvania. She has been published in peer-reviewed journals such as *Trauma Nurse*, *Orthopedic Nurse*, and *Western Journal of Nursing Research.*

Acknowledgments

There are a lot of people to thank in a project of this scope. First and foremost, I would like to thank Ruth Woodrow for the honor to continue her vision on such a quality textbook.

I would also like to thank Adam James, who served as the pharmacist consultant and co-author on this project to make sure we got it right. I have known Adam for several years and I'm very impressed with his work ethic, knowledge, and professionalism. His updates with the latest and greatest information concerning specific drugs and dosages have been truly appreciated.

Co-author Liz Katrancha deserves a big thank you for being the nursing consultant to make sure we keep the textbook patient centered, clinically applied, and up to date. I have had the pleasure of working with Liz on several projects and her attention to detail and quality of work are greatly appreciated.

Last but certainly not least, I want to personally thank all the people at Cengage that have worked on this project. Of special mention is Andrea Henderson, my editor, who has given me tremendous support and encouragement over the years. Debra Myette-Flis, the learning designer, deserves a special thank you for her tremendous assistance, organizational skills, professional knowledge, and guidance in helping to make this project a joy on which to work. Finally, Ken McGrath, who oversees this multifaceted revision process with technical expertise and is always great to work with.

Bruce J. Colbert

Reviewers

The authors and Cengage wish to acknowledge and sincerely thank the following reviewers.

Eleonora Alvarado, RN, MHA, CPC
Assistant Professor
Nashville State Community College

Jessica Duncan, BS, NRP C-CP
EMS Faculty
Southern Union State Community College

Roseanna McGinn MBA-HCA, RHIT
Director of Health Information Technology
University of New Mexico Gallup

Heather Morris, RHIA, BHS, CDIP, CCS-P
Trident Technical College

Tiffany Rosta, CMA
Allied Health Instructor, Clinical Coordinator
Laurel Technical Institute

Donna White, RHIA, CCS
Instructor
Haywood Community College

PART 1

Introduction to Pharmacologic Principles

Chapter 1

Consumer Safety and Drug Regulations

Key Terms and Concepts

Controlled substances
Drug Enforcement Administration (DEA)
Drug standards
Food and Drug Administration (FDA)
National Drug Code (NDC) Directory
Orphan drugs
Over-the-counter (OTC) medication

Objectives

Upon completion of this chapter, the learner should be able to:

1. Explain what is meant by drug standards.
2. Summarize the historical development of pharmacology.
3. Name the first drug law passed in the United States for consumer safety and give the year it was passed.
4. Summarize the provisions of the Federal Food, Drug, and Cosmetic Act of 1938 and its amendments.
5. Interpret what is meant by *USP/NF*.
6. Summarize the provisions of the Controlled Substances Act of 1970.
7. Contrast the responsibilities of the FDA and DEA.
8. Define *orphan drug*.
9. Differentiate between controlled substance schedules C-I through C-V.
10. State several responsibilities you have in administering medications as a direct result of the three major drug laws described in this chapter.

Your decision to pursue a career in the health care field probably took a great deal of thought. No doubt you have questioned whether you will be able to handle the unique situations that arise in a clinic, health care facility, or physician's office. Have you ever stopped to consider the impact *you* will make on the lives of others as a health care professional? Not only can you make a tremendous difference in the facility where you work, but you can also have a positive impact on your friends and family, as well as the patient or client.

It is inevitable that you will receive many questions about medications, prescriptions, and drug therapy. A great majority of patients are far too inhibited to tell their physicians that there are things they do not understand about their medications.

They feel much more at ease discussing their questions with health care professionals. Your potential for informing others with knowledgeable answers about medications can be quite an asset!

The key to reaching that potential is having knowledgeable answers coupled with a serious, responsible attitude about all aspects of drug therapy. Consider yourself a potential prime resource of medication information for your friends, family, and future patients as you begin to examine the foundations of facts about drugs. It may be necessary for you to clarify some of the layperson misunderstandings about the legalities of dispensing medications. Consider the following misconceptions and facts.

False	**Fact**
Only nurses can give medications to patients.	Trained and certified health care professionals who may legally give medications include physicians; physician assistants; paramedics; clinical medical assistant; unlicensed assistive personnel; practical, vocational, and registered nurses; and other allied health specialists such as respiratory therapists and pharmacists.
Only physicians may write prescriptions.	Dentists, physicians, physician assistants, veterinarians, nurse practitioners, and registered pharmacists may write prescriptions for their specific field of work, as governed by state law. For example, veterinarians write prescriptions only for animal use.
Prescriptions are required for narcotics only.	Specific drugs ruled illegal to purchase without the use of a prescription include the following: Those that need to be controlled *because they are addictive and tend to be abused and dangerous* (e.g., depressants, stimulants, psychedelics, and narcotics) Those that may cause dangerous health threats from side effects if taken incorrectly (e.g., antibiotics, cardiac drugs, and tranquilizers)
All drugs produced in the United States are made in federally approved laboratories.	Numerous illegal laboratories that produce illicit substances such as methamphetamines exist and operate within the United States today.
Prescriptions cannot be written for over-the-counter (OTC) medications.	Prescribers are able to write prescriptions for any FDA-approved medication and all OTC medications. Many times medications that were once available by prescription only are now available over the counter. Additionally, if a prescriber wishes for the patient to take an OTC medication differently from the instructions on the label, a prescription can be written to help the patient with compliance. Often OTC medications obtained via a prescription are covered by insurance and are therefore much more affordable, especially for older adults.
All herbal medicines and dietary supplements are safe.	Herbal remedies and other dietary supplements are not approved or manufactured per production standards regulated by the Food and Drug Administration (FDA) and may have serious interactions with prescribed medications. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. The FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market and against marketed products that make false or misleading claims.

Drug History

Have you wondered how the numerous types of natural drugs and even immunizations ever came to be? Who were the first people to begin to treat diseases with drugs and who was the first person to create synthetic scientifically made medications? What were the major discoveries that led to better therapy outcomes? All these questions are important in understanding pharmacology and how it evolved over time to achieve this amazing degree of success that we have in treating patients with medications today. This success includes improving not only on life expectancy but also on quality of life.

From the very first documented use of "pharmacology" in ancient Egypt, where they used substances such as berries, beer, poppies, salt, and even crushed precious stones to treat ailments, it was clear that humans were determined to overcome diseases by any means necessary. Please refer to the timeline that shows some of the most important developments, discoveries, dates, people, and even setbacks in the history of pharmacology as we know it today.

Pharmacology Timeline

Date	Pharmacologic Event
16th century BCE	Earliest documented pharmacologic examples found recorded on papyri from ancient Egypt
2nd century BCE	Earliest evidence of actual "prescriptions"
1st century BCE	Greek physician Dioscorides writes the *De Materia Medica*, which is considered the most influential work in the history of western pharmacology
1885	Pasteur develops precursor to rabies vaccine Oswald Schmiedeberg, known as the founder of modern pharmacology, publishes *Outline of Pharmacology*
1897–1899	Aspirin discovered and first marketed for use
1905	German chemist Alfred Einhorn discovers procaine, giving it the trade name Novocaine (aka Novocain)
1906	The Pure Food and Drug Act passed in United States
1922	Insulin first used to treat diabetes
1928	Alexander Fleming discovers penicillin
1936	Chemotherapy first used to treat cancer
1937	Over 100 people die in the United States of a sulphanilamide elixir, leading to passage of the Federal Food, Drug, and Cosmetic Act in 1938
1953	Watson and Crick describe the structure of DNA
1960	First contraceptive pill
1958–1960	Thalidomide crisis where approximately 10,000 babies were born with deformities after thalidomide was used to treat morning sickness; this led to passage of a drug amendment act establishing the Food and Drug Administration in 1962
1969	Ibuprofen developed in Great Britain
1991	FDA approves the first-ever treatment for hepatitis C (interferon alpha-2b)
2000	First draft of the human genome released to public; this sets the stage for genetically targeted drugs
2017	Shingrix, the vaccine to treat shingles, approved
2020–2021	Several vaccines developed in an attempt to mitigate the COVID-19 global pandemic
2023–2024	First respiratory syncytial virus (RSV) vaccine approved.

Drug Laws

Individuals have been using substances and drugs for healing purposes for centuries. Due to scientific advances and changes in our society in the last century, consumer safety has become a critical issue. During the 1900s, laws were passed that specifically addressed the matter of safely dispensing drugs in the United States.

Drug standards are rules set to assure consumers that they get what they pay for. The law says that all preparations called by the same drug name must be of *uniform strength*, *quality*, and *purity*.

Because of drug standardization, when you take a prescription to be filled, you are assured of getting the same basic drug, in the same amount and of the same quality, regardless of the pharmacy or the part of the country where you take the prescription. According to drug standards, drug companies must not add other active ingredients or varying amounts of chemicals to a specific drug preparation. They must meet the drug standards (federally approved requirements) for the specified strength, quality, and purity of the drug.

In the market of illegal (illicit) drugs, the lack of enforcement of drug standards poses danger to the consumer. With no controls on the quality of illegal drugs, many deaths have occurred from overdose. Consider the person using heroin, accustomed to very poor-quality heroin, who accidentally overdoses when given heroin of a much higher quality from a new source. In general, across the country, opioid and other drug overdoses have become a major problem. It is important to be aware of the problems that can arise when certain drugs are abused.

The laws that have evolved to provide consumer safety can be summed up by three major acts. They are described in the order they became necessary for consumer safety, beginning with the 1906 Pure Food and Drug Act.

The importance of the timing of the 1938 Federal Food, Drug, and Cosmetic Act should be noted. It came about as the answer to a disastrous occurrence in 1937. A sulfa preparation, not adequately tested for safety, was responsible for 100 deaths that year. Thus, the need was recognized for more proof of the safety of new drugs. Several amendments were later added, such as the 1962 amendment due to the thalidomide crisis. In 2023, after a Massachusetts company was found guilty of failing to notify consumers of defects in products (such as Dexamethasone) it manufactured, the law was used to prohibit the company from manufacturing medications.

1906 Pure Food and Drug Act

First government attempt to establish consumer protection in the manufacture of drugs and foods.

Required all drugs marketed in the United States to meet minimal standards of strength, purity, and quality.

Demanded that drug preparations containing dangerous ingredients have a labeled container indicating the ingredient. Originally there were 11 “dangerous” ingredients, such as morphine.

Established two references of *officially* approved drugs. Before 1906, information about drugs was handed down from generation to generation. No official written resources existed. After the 1906 legislation, two references specified the official U.S. standards for making each drug. These references, listed here, have since been combined into one book, referred to as the *USP/NF*:

- *United States Pharmacopeia (USP)*
- *National Formulary (NF).* This book can be accessed online with a subscription and is really meant for prescribers.

1938 Federal Food, Drug, and Cosmetic Act and Amendments of 1951, 1962, and 1972

Established the **Food and Drug Administration (FDA)** under the Department of Health and Human Services to enforce the provisions of the act.

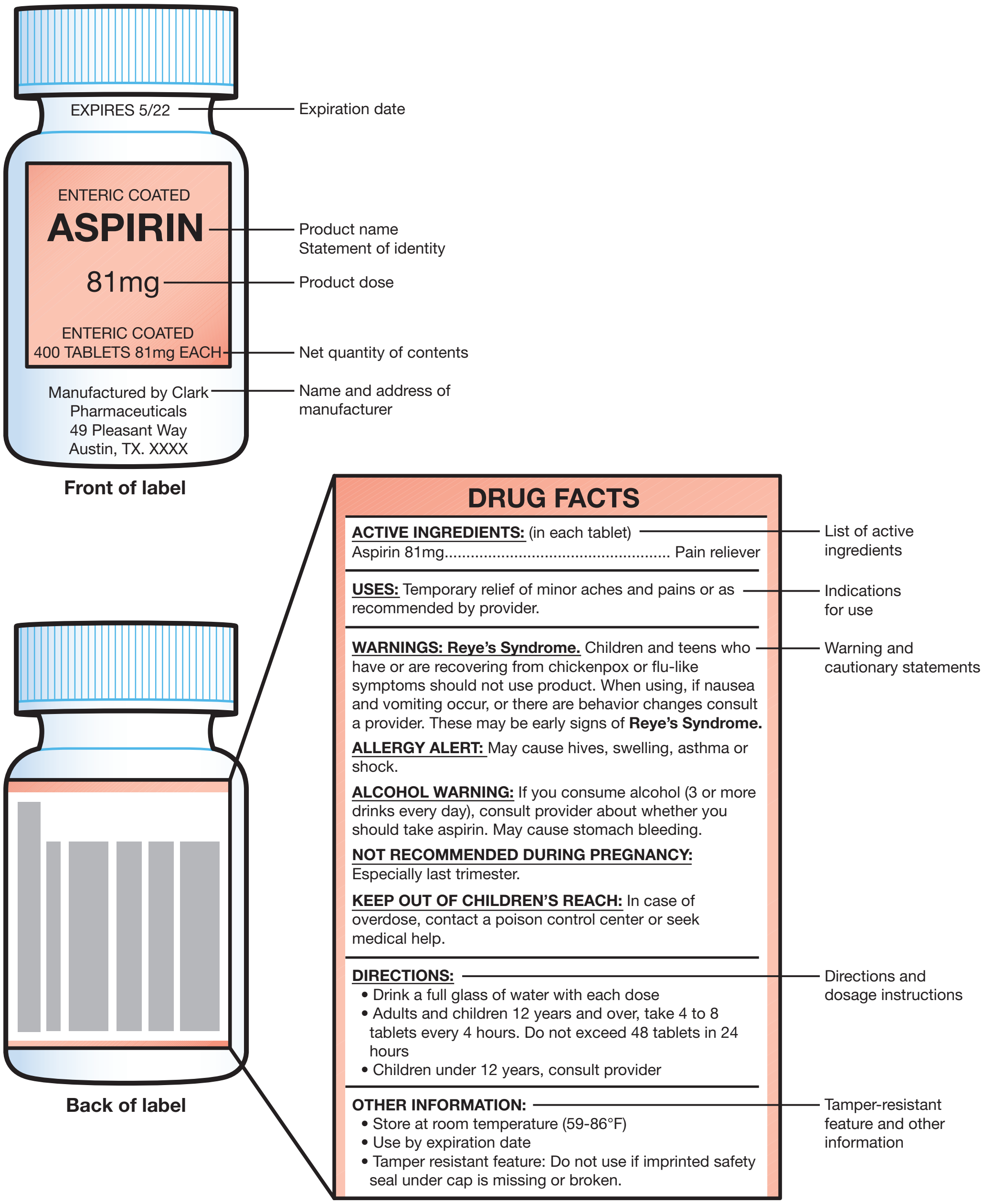
Established *more specific* regulations to prevent adulteration of (tampering with) drugs, foods, and cosmetics:

- All labels must be accurate and must include a listing of all active and inactive ingredients. Figure 1-1 shows an example of required product information for an **over-the-counter (OTC) medication** (no prescription [Rx] needed).
- All new products must be approved by the FDA before public release.
- "Warning" labels must be present on certain preparations, for example, "may cause drowsiness," "may cause nervousness," and "may be habit-forming."
- Certain drugs must be labeled with the legend (inscription) "Caution—federal law prohibits dispensing without a prescription." Thus, the term *legend drug* refers to such preparations. The act also designated which drugs can be sold without a prescription.
- Prescription and nonprescription drugs must be shown to be *effective* as well as *safe*.
- In 1972, the **National Drug Code (NDC) Directory** was established. This provided the FDA with a list of all drugs manufactured for commercial distribution. Each drug is identified by an NDC number, made up of three parts (Figure 1-2).
  - The first part is five numbers and identifies the manufacturer.
  - The second part is four numbers and identifies the drug.
  - The third part is two digits and identifies the package size.
    - Example: 00406-0123-01; note it is a common practice to omit a leading zero in the first or second part of the NDC number, so this drug could also be written as 0406-123-01.

The five schedules of **controlled substances** are arranged with those with the highest potential for abuse at level I and those with the lowest abuse potential at level V. It should be noted that even those drugs in class level V have more potential for abuse than most drugs. Additionally, the lower the number, the stricter are the restrictions for control by the DEA. Therefore, it makes sense that Schedule I drugs are illegal and are not approved for medicinal purposes in the United States.

Drugs are frequently added, deleted, or moved from one schedule to another. If, for example, the DEA determines that drug A is becoming more of a societal problem, with an increased incidence of overdoses, drug A may be moved from the C-IV schedule to C-III. It is extremely important that the health care professional keep informed of any changes in drug scheduling. For the most part, using the most current drug reference book will keep you up to date.

You will recognize the schedule of a particular controlled substance by noting a *C* with either *I*, *II*, *III*, *IV*, or *V* after it. Some references show the capital *C* with the Roman numeral inside the curve of the *C* (CIV). Labels on controlled substances are also designated with a *C* and a Roman numeral to indicate their level of control. Drug inserts (information leaflets accompanying drugs) are also marked with a *C* and the appropriate schedule number (Table 1-1 and Figure 1-3).


EXPIRES 5/22
Expiration date
ENTERIC COATED
ASPIRIN
Product name
Statement of identity
81mg
Product dose
ENTERIC COATED
400 TABLETS 81mg EACH
Net quantity of contents
Manufactured by Clark Pharmaceuticals
49 Pleasant Way
Austin, TX. XXXX
Name and address of manufacturer
Front of label
Back of label
List of active ingredients
Indications for use
Warning and cautionary statements
Directions and dosage instructions
Tamper-resistant feature and other information

DRUG FACTS

ACTIVE INGREDIENTS: (in each tablet)
Aspirin 81mg.. Pain reliever

USES: Temporary relief of minor aches and pains or as recommended by provider.

WARNINGS: Reye's Syndrome. Children and teens who have or are recovering from chickenpox or flu-like symptoms should not use product. When using, if nausea and vomiting occur, or there are behavior changes consult a provider. These may be early signs of **Reye's Syndrome.**

ALLERGY ALERT: May cause hives, swelling, asthma or shock.

ALCOHOL WARNING: If you consume alcohol (3 or more drinks every day), consult provider about whether you should take aspirin. May cause stomach bleeding.

NOT RECOMMENDED DURING PREGNANCY: Especially last trimester.

KEEP OUT OF CHILDREN'S REACH: In case of overdose, contact a poison control center or seek medical help.

DIRECTIONS:
- Drink a full glass of water with each dose
- Adults and children 12 years and over, take 4 to 8 tablets every 4 hours. Do not exceed 48 tablets in 24 hours
- Children under 12 years, consult provider

OTHER INFORMATION:
- Store at room temperature (59-86°F)
- Use by expiration date
- Tamper resistant feature: Do not use if imprinted safety seal under cap is missing or broken.

Figure 1-1 Consumer medication labels contain valuable information for safe and effective use of the drug.

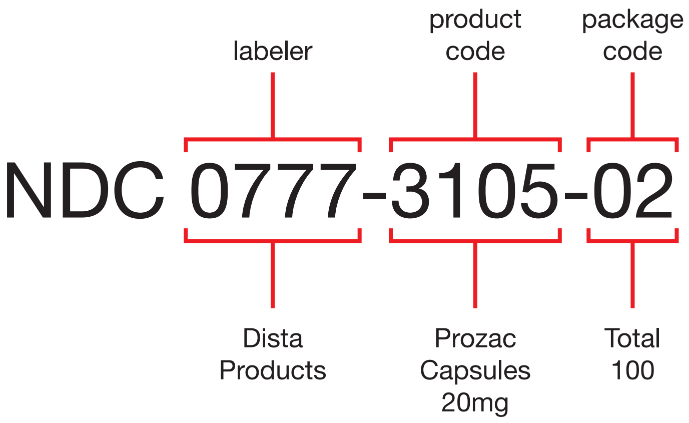

labeler
product code
package code
NDC 0777-3105-02
Dista Products
Prozac Capsules 20mg
Total 100

Figure 1-2 NDC code for the drug Prozac.

1970 Controlled Substances Act

Established the **Drug Enforcement Administration (DEA)** as a bureau of the Department of Justice to enforce the provisions of the act.

Set much tighter controls on a specific group of drugs: *those that were being abused by society*; the name of the act indicates that such *substances needed to be controlled*. These substances include depressants, stimulants, psychedelics, narcotics, and anabolic steroids. The act:

- Isolated the abused and addicting drugs into five levels, or schedules, according to their medical value, harmfulness, and potential for abuse or addiction: C-I, C-II, C-III, C-IV, and C-V.
- Demanded security and accountability related to controlled substances; anyone (e.g., pharmacists, hospitals, physicians, and drug companies) who dispenses, receives, sells, or destroys controlled substances must keep on hand special DEA forms, indicating the exact current inventory and a two-year inventory of every controlled substance transaction.
- Set limitations on the use of prescriptions; guidelines were established for each of the five schedules of controlled substances, regulating the number of times a drug may be prescribed in a six-month period as well as for which schedules prescriptions may be phoned in to the pharmacy and so on.
- Demanded that each prescriber of these substances register with the DEA and obtain a DEA registration number, to be present on their prescriptions of controlled substances; drug manufacturers must also be registered and identified with their own DEA numbers, as must pharmacists, physicians, veterinarians, and so on.

Table 1-1 Five Schedules of Controlled Substances

Schedule Number	Abuse Potential and Legal Limitations	Examples of Substances
1, CI	High abuse potential Not approved for medical use in the United States (discussed in Chapter 20)	heroin, LSD, methamphetamine, ecstasy
2, CII	High abuse potential May lead to severe dependence Written prescription only (or electronic prescription that meets DEA standards) Some states do not allow phoning or faxing in of prescriptions by the office health care professional; in an emergency, physician may phone in, but handwritten prescription must go to the pharmacy within seven days No refills without new written prescription Electronic prescribing systems may be used for C-II prescriptions, if both the prescriber and the pharmacy are verified to have approved computer systems to send and receive these types of prescriptions All C-II prescriptions are uploaded to the state's (if available) prescription drug monitoring program (PDMP)	morphine, codeine, methadone, Percocet, Dilaudid, Ritalin, OxyContin, meperidine (Demerol), hydrocodone with Tylenol
3, CIII	May lead to moderate to low dependence Written, faxed, or verbal (phoned in) prescription, by physician only May be refilled up to five times in six months All C-III prescriptions are uploaded to the state's (if available) prescription drug monitoring program (PDMP)	codeine, anabolic (muscle-building) steroids

Schedule Number	Abuse Potential and Legal Limitations	Examples of Substances
4, CIV	Lower abuse potential than the previous schedules Prescription may be written out by the health care professional but must be signed by the physician Prescription may be phoned in by the health care professional or faxed May be refilled up to five times in six months All C-IV prescriptions are uploaded to the state's (if available) prescription drug monitoring program (PDMP)	Valium, Ativan, Xanax, phenobarbital, Librium, Restoril, Ambien
5, CV	Low abuse potential compared to the previous schedules Consists primarily of preparations for cough suppressants containing codeine and preparations for diarrhea (e.g., diphenoxylate) May be refilled up to five times in six months	promethazine with codeine, Cheratussin AC, Lomotil

Note: This control schedule can vary from state to state. Some states may have stricter schedules than the federal regulations. You must be aware of the regulations in your area.

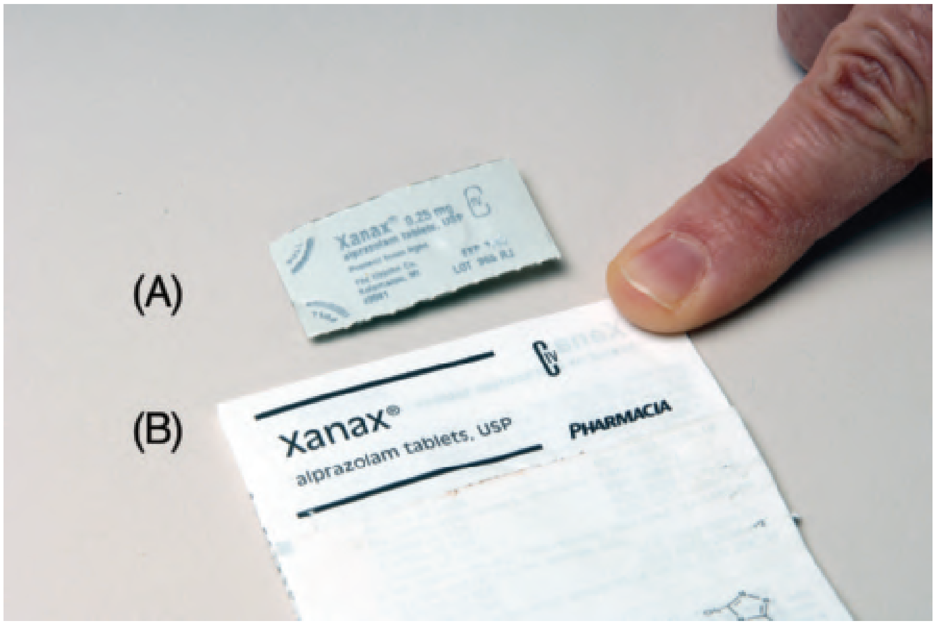


Figure 1-3 Controlled substance schedule numbers appear in a variety of drug information resources, including (A) drug packages and (B) drug inserts. Schedule numbers are also found in drug reference sources.

Clinical Application

Although many other drug laws exist, there are two significant pieces of drug legislation that are important to mention here. The 1983 Orphan Drug Act gives pharmaceutical companies financial incentives to develop medications for diseases that affect only a small number of people. This encourages the companies to develop **orphan drugs** that would otherwise be of low profitability. The other legislation is the strangely named Omnibus Budget Reconciliation Act (OBRA) of 1990. This act mandates that all OTC drugs a patient is taking must be documented as part of the medical record. OBRA also mandates that pharmacists provide drug use review and patient counseling before dispensing prescriptions to a patient.

FDA and DEA

The increase in the number of drugs produced for marketing brought dangers to the public. The federal FDA was established to ensure that some basic standards would be followed. Its responsibilities include:

- Overseeing testing of all proposed new drugs before they are released into the U.S. market
- Inspecting plants where foods, drugs, medical devices, or cosmetics are made
- Reviewing new drug applications and petitions for food additives
- Investigating and removing unsafe drugs from the market
- Ensuring proper labeling of foods, cosmetics, and drugs

When the need for better control of addictive drugs became urgent, the FDA had its hands full just trying to enforce basic drug standards. It became imperative to set up a new department, the DEA, in 1970 to handle all the needs and safety controls for the more dangerous drugs. Thus, the two agencies—FDA and DEA—were established with their own specific areas of drug control.

As a health care professional and an informed citizen, you must be aware of the latest developments concerning these two agencies. Hardly a week goes by without mention of the activities of the FDA or the DEA in the news. You should be able to recognize their separate areas of control.

FDA

Concerned with general safety standards in the production of drugs, foods, and cosmetics.

Responsible for approval and removal of products on the market. *Special note on drug withdrawals:* In rare cases, the FDA may need to reassess and change its approval decision on a drug. A conclusion that a drug should no longer be marketed is based on the nature and frequency of the adverse events and how the drug's benefit and risk balance compares with treatment alternatives. When the FDA believes that a drug's benefits no longer outweigh its risks, the agency will ask the manufacturer to withdraw the drug. Interestingly, the FDA does not have the legal authority to withdraw a marketed drug product itself.

DEA

Concerned only with controlled substances.

Enforces laws against drug activities, including illegal drug use, dealing, and manufacturing.

Monitors need for changing the schedules of abused drugs.

Health Care Professionals and the Law and Ethics

In some ways, you will be as involved as the physician in observing the restrictions of the drug laws. You will have the responsibility of keeping accurate records of the medications dispensed. You will maintain the supply of drugs at your facility. If you work in a physician's office, a clinic, or an ambulatory care setting, you will also be involved with phoning in prescriptions and securing prescription forms at your facility. You must act ethically to ensure that the ordered medications are given in the appropriate amount to the appropriate patient.

The following guidelines should be followed by the health care professional involved in dispensing medications:

1. Keep a *current* drug reference source available at all times. You should be able to readily identify substances that are controlled by the DEA.
2. Keep controlled substances locked securely. Double-locking is required in most situations. This means:
   a. Placing the drugs in a locked safety box
   b. Placing the locked box in a cupboard that is also locked
3. Conceal and secure prescription pads at your office, clinic, or facility. Do not leave pads out in the open, especially in patient examination rooms. The prescription pads, with the physician's DEA registration number, are a possible source of fraud and drug tampering when forged and used illegally. Keep the pads locked up and in a designated location (e.g., a drawer), out of the public areas of the office or nursing station. One of the most common ways prescriptions are forged is through a stolen prescription pad.
4. Keep accurate records of each controlled substance administered, received, or destroyed at your facility. These records, as well as the records from the previous two years, must be available at all times. Properly destroy expired drugs and old records. Two employees are typically required to count all controlled substances at the beginning and end of each shift. In some facilities (particularly government-run facilities) unannounced counts are conducted by designated inspectors from different areas of the facility. In community pharmacies, double-counting controlled medications before dispensing is standard practice, and monthly counts must be completed and compared against dispensing records.
5. Be responsible for keeping up to date with current news of the activities of the FDA and the DEA. If working for a physician, monitor the DEA registration renewal date. Keep informed of any changes in the scheduling of controlled substances. Some states have legalized marijuana (a Schedule 1 drug); however, federal law continues to label it as illegal. Additionally, most employers have policies against the use of marijuana.
6. Establish a working rapport with a pharmacist. A local pharmacist is an excellent resource for you when you are unsure of your legal responsibilities with drugs or have any uncertainties about drug therapy.
7. If you work in an office, maintain a professional rapport with the pharmaceutical representatives who leave drug samples there. As part of the Affordable Care Act, the Sunshine Act now requires reporting of compensation and gifts paid to physicians by pharmaceutical representatives. It is important that you are aware of the ethical dilemma that may occur when a physician is "rewarded" or compensated for prescribing certain medications.

Chapter Review Quiz

Complete the following statements

1. The first major U.S. drug law was passed in the year ________ and was called the ______________________

   ____

2. USP stands for ____
3. NF stands for ____
4. Which drug law established the USP and NF (which are now one)? ______________________
5. The agency that requires you to keep a record of each controlled substance transaction is the ____________

   ____

6. Schedule C-______________________________ has the lowest potential for abuse.
7. How long must you keep an inventory record of each controlled substance transaction at your office?

   ____

   ____

8. Three responsibilities of the FDA include: ______________________________

   ____

   ____

9. What types of drugs are listed in the C-V schedule? ______________________________

   ____

10. What method is recommended for securing the controlled substances at your office? ______________

    ____

11. If a patient calls to request a refill of a Percocet (C-II) prescription, how would you reply? ____________

    ____

12. A patient has a rare disease that requires medication for only a small population of patients. Which act has allowed their drug to be produced even though it is not profitable to the pharmaceutical industry?

    ____

13. A patient calls into the office asking for a new prescription for a narcotic medication that they have been taking for six months. You bring up the chart and notice that they have been requesting new prescriptions every 23 days, whereas the medication should last 30 days. Additionally, the patient also mentions that they feel in need of a higher dose and get agitated and irritable when you tell them that they will need an appointment. What do you think of this? What should you do?
14. Each drug is given a ______________ number to identify the manufacturer, the drug, and the package size.

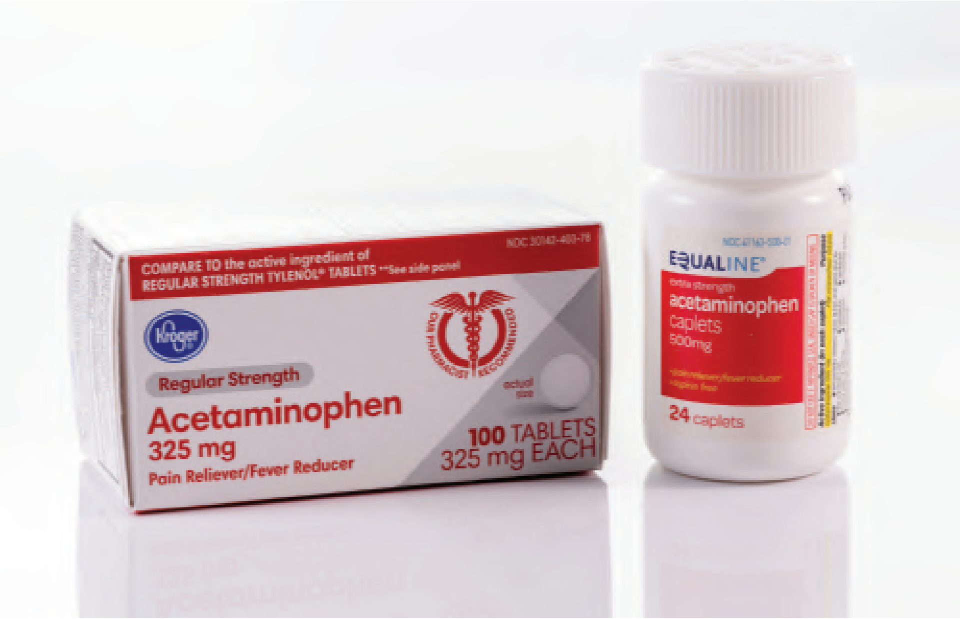
    a. FDA
    b. USP
    c. DEA
    d. NDC

15. Answer the questions concerning the following three drug labels:

a. Which drug(s) require(s) a prescription?

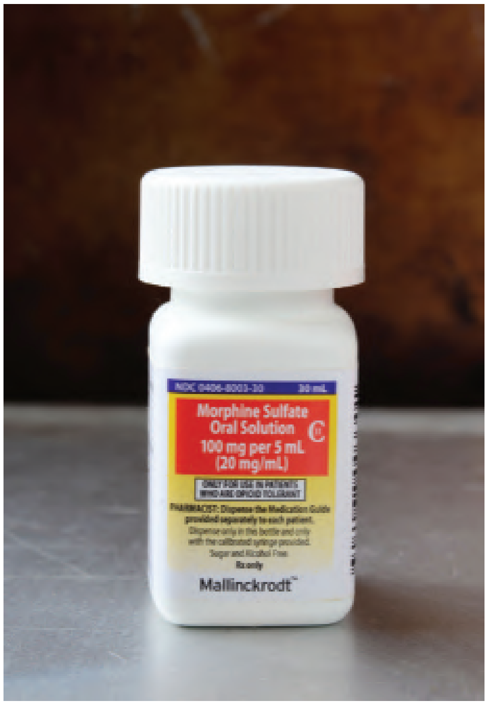
b. Which drug(s) can be bought without a prescription?

c. Which drug(s) require(s) a DEA number?


COMPARE TO the active ingredient of REGULAR STRENGTH TYLENOL® TABLETS **See side panel
Kroger
Regular Strength
Acetaminophen
325 mg
Pain Reliever/Fever Reducer
100 TABLETS
325 mg EACH
EQUALINE
acetaminophen
caplets
500mg
24 caplets

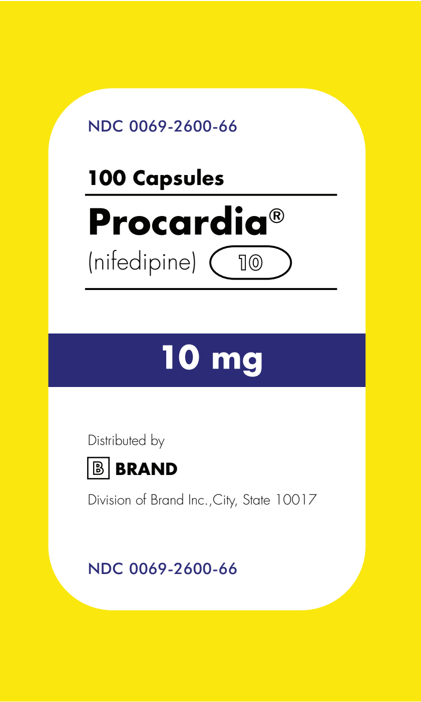
Steve Heap/Shutterstock.com.

(A)


NDC 0406-8003-30
30 mL
Morphine Sulfate
Oral Solution
100 mg per 5 mL
(20 mg/mL)
ONLY FOR USE IN PATIENTS WHO ARE OPIOID TOLERANT
Rx only
Mallinckrodt™

Margaret M Stewart/Shutterstock.com.

(B)



NDC 0069-2600-66

100 Capsules

Procardia®
(nifedipine) 10

10 mg

Distributed by
BRAND
Division of Brand Inc.,City, State 10017

NDC 0069-2600-66

(C)

16. Drug standards ensure consistency in all the areas EXCEPT

a. strength
b. purity
c. quality
d. size

17. The Federal Food, Drug, and Cosmetic Act of 1938 established which agency?

a. NDC
b. DEA
c. FDA
d. USP

18. The earliest recorded use of drugs occurred during which civilization?

a. Egyptian
b. Greek
c. Roman
d. Aztec

Chapter 2

Drug Names and References

Key Terms and Concepts

Actions
Adverse reactions
Cautions
Classifications
Contraindications
Generic names
Indications
Interactions
Legend drug
Official name
Off-label medication
Pharmacology
Prototype
Side effects
Tall Man Lettering
Trade names

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe drug classification systems.
2. Differentiate among the following drug names: generic name, official name, trade name, and chemical name.
3. Explain what is indicated by a number included in a drug trade name (e.g., Tylenol No. 3).
4. Explain the purpose of Tall Man Lettering.
5. Explain the restrictions of drug sales implied by the following: over-the-counter (OTC) drug, legend drug, off-label drug use, and controlled substance.
6. Define the various terms indicating drug actions contained in reference sources.
7. Describe drug references available today.
8. List characteristics that you consider important in choosing the best drug reference.

Pharmacology can be defined as the study of drugs and their origins, nature, and properties, as well as their effects on living organisms. We need to know why drugs are given, how they work, and what effects to expect. The thousands of drug products on the market would make this subject difficult to tackle if it were not for:

- Numerous drug references, geared to a variety of levels of readers, from layperson to pharmacist
- Grouping of drugs under broad subcategories
- Continuity in the use of basic identifying terms for the names and actions of drugs

Classifications

Each drug can be categorized under a broad *subcategory*, or *subcategories*, called **classifications**. Although drugs can be classified in several different ways, grouping them together according to their therapeutic use is most helpful to the health care professional. Drugs that affect the body in similar ways are listed in the same classification. Drugs that have several types of therapeutic effects fit under several classifications. For example, aspirin has a variety of effects on the body. It may be given to relieve pain (analgesic), to reduce fever (antipyretic), to reduce inflammation of tissues (anti-inflammatory), or as an anti-platelet (anti-thrombotic agent). Therefore, aspirin is categorized under four classifications of drugs (as shown in parentheses).

Another drug, cyclobenzaprine (Flexeril), however, is known to be used for only one therapeutic effect: to relieve muscle spasms. Flexeril, therefore, is listed only under the one classification of muscle relaxant.

An example of a class of medications that are approved for more than one use is the GLP-1 agonists such as Semaglutide (Ozempic). Although this class of drugs is approved to treat Type 1 diabetes, it is also approved as a weight loss drug.

Examples of some common drug classifications are listed in Table 2-1. Are you familiar with any of them already?

Clinical Application

What is the difference between drug classifications and drug classes? While drug classifications place drugs in broad categories according to their therapeutic use, under that category can be several types of drug classes that are grouped together based on how they work or their mechanism of action. For example, say the drug classification is hypertensive agents; under this classification are several drug classes (beta-blockers, alpha blockers, calcium channel blockers, ace inhibitors, etc.)—all different drug classes because they treat hypertension by different means.

Table 2-1 Common Drug Classifications and Examples

Classification	Therapeutic Use	Drug Example(s)
1. Lipid-lowering agents	Lower low-density lipoprotein (LDL) cholesterol	simvastatin, atorvastatin, rosuvastatin
2. Antidepressants	Improve symptoms of depression; also used for anxiety and other neurological disorders	escitalopram, sertraline, paroxetine, venlafaxine
3. Narcotic analgesics	Relieve severe pain	hydrocodone with acetaminophen, oxycodone, oxymorphone, fentanyl
4. Antihyper-tensives	Lower blood pressure	lisinopril, enalapril, valsartan
5. Diuretics	Increase urinary output	furosemide
6. Antidiabetics	Reduce blood glucose (sugar) levels	insulin, metformin, glipizide, Jardiance, Moumjaro
7. Antibiotics	Eliminate infection	amoxicillin, cephalexin, doxycycline
8. Anticoagulants	Decrease clotting in blood	warfarin, Xarelto

The second part of this text compares the characteristics of the various major drug classifications. In each chapter, as a classification is explained, you will be presented with general information to associate drugs of that classification, including:

- Therapeutic uses
- Most common side effects
- Precautions to be used
- Contraindications (when *not* to use the drug)
- Interactions that may occur when taken with other drugs or foods
- Some of the most common product names, their usual dosages, and comments on administration

You may also be given a **prototype** of each drug classification. A prototype is a *model example*, a drug that typifies the characteristics of that classification. For example, propranolol (Inderal) is the prototype of the beta-adrenergic blockers that will be explained in the cardiovascular chapter.

You can find the classification, as well as the various names, of a drug by referring to a drug reference source.

Identifying Names

Drug names can seem very complicated because a single drug will have many names attached to it. Four specific names can apply to each approved drug:

1. ***Generic name***
   a. Common or general name assigned to the drug by the United States Adopted Name (USAN) council
   b. Differentiated from the trade name by initial lowercase letter
   c. Never capitalized
2. ***Trade name*** (also known as proprietary or brand name since it is owned by a company)
   a. The name by which a pharmaceutical company identifies its product
   b. Copyrighted and used exclusively by that company
   c. Distinguished from the generic name by capitalized first letter
   d. Often shown on labels and references with the symbol ® (for "registered" trademark) after the name
3. ***Chemical name***
   a. The exact molecular formula of the drug
   b. Usually a long, very difficult name to pronounce
   c. Of little concern to the health care professional
4. ***Official name***
   a. Name of the drug as it appears in the official reference, the *United States Pharmacopeia/National Formulary (USP/NF)*
   b. Generally, the same as the generic name

The use of **generic names** and **trade names** for drugs can be compared to the various names of grocery products. Two examples of generic names are orange juice and detergent. Whereas trade names for orange juice are Tropicana and Minute Maid, Cheer and Tide are trade names for detergents. Although there is only one generic name, there may be many trade names marketed by different companies.

When a company produces a new drug for the market, it assigns a generic name to the product. After testing and approval by the Food and Drug Administration (FDA), the drug company gives the drug a trade name (often something short and easy to remember when advertised). For five years, from the time the company submits a *new drug application (NDA)* to the FDA for approval, the company has the exclusive right to market the drug. Once approved, the drug is listed in the *USP/NF* by an **official name**, which is usually the same as the generic name. After five years have passed and the patent has expired (although patent extensions are requested and frequently granted), other companies may begin to combine the same chemicals to form that specific generic product for marketing. Each company will assign its own specific trade name to the product, or the drug can be offered simply by its generic name and strength, such as acetaminophen 325 mg. Table 2-2 compares the names for two drugs.

Concerning prescription drugs, most states have enacted legislation encouraging physicians to let pharmacists substitute less expensive *generic equivalents* for prescribed brand name drugs. Specific provisions of drug *substitution laws* vary from state to state.

The physician may indicate "no substitutions" on the prescription, usually indicated by a *dispense as written (DAW) order*. Often physicians have preferences for certain products, or patients may be difficult to stabilize on a certain class of medications (such as thyroid preparations). Even though the drug contents are the same, the "fillers," or ingredients that are used to hold the preparation together, may be slightly different. This difference in fillers may affect how quickly the drug dissolves or takes effect. Dyes in some products may alter effects in some patients who are sensitive by leading to an allergic response.

Many products are combinations of several generic components. You will recognize this when you have several generic names (not capitalized) and their corresponding amounts listed under one trade name (capitalized). Examples are given in Table 2-3.

Table 2-2 Comparison of Drug Names

Generic Name	Chemical Name	Trade Names (Drug Company)
doxycycline hyclate	2-naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11, 12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-, (4S,4aR,5S,5aR,6R,12aS)-(564-25-0)	Vibramycin (PD-RX Pharmaceuticals) doxycyclinehyclate[a] (West-Ward)
chlordiazepoxide hydrochloride	7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazephine-4-oxide hydrochloride	Librium

[a] Some companies simply elect to market the product by the generic name.

Table 2-3 Examples of Combination Drugs

Trade Name	Generic Name and Amount
Dyazide (used to treat high blood pressure)	hydrochlorothiazide 25 mg/triamterene 37.5 mg
Glucovance (used to treat type 2 diabetes mellitus)	glyburide 1.25 mg/metformin 250 mg glyburide 2.5 mg/metformin 500 mg glyburide 5 mg/metformin 500 mg
Robitussin DM 5 mL syrup	dextromethorphan 10 mg/guaifenesin 100 mg

Patient Education

Patients may ask you about the difference between generic and trade (brand) name products. The FDA regulates the manufacturing of generic drugs, so patients can be assured that they are safe and cost-effective alternatives. Generally, trade name products are more expensive, although the basic active ingredients (drug contents) are the same as those in the generic. The higher price helps to pay for the costs of drug development and advertisements promoting the trade name. (Can you think of certain trade names that are heavily advertised in television commercials or on the Internet?)

Because generic drug equivalents may exist for both prescription and OTC drug products, it is often economically wise to check for medicines that have the same generic components and strengths. For example, several cough syrups may have exactly the same contents, but the prices may vary widely.

Read and compare all ingredients on the labels.

It should be noted that a number may be part of the trade name. The number often refers to an amount of one of the generic components and helps to differentiate it from another nearly identical product. Identify the significance of the numbers in comparing the following trade names:

Trade Name	Generic Name and Amount
Tylenol No. 2	acetaminophen 300 mg; codeine 15 mg
Tylenol No. 3	acetaminophen 300 mg; codeine 30 mg
Tylenol No. 4	acetaminophen 300 mg; codeine 60 mg

Note that each product contains the same amount of acetaminophen, with varying amounts of the controlled substance codeine. *The larger the number in the name, the greater the amount of controlled substance present.*

Many drug errors have occurred because the trade name was misinterpreted for the number of tablets to be given. So . . .

Be certain you can clearly read and understand the order!

Another type of drug error involves preventable allergic reactions to one of the generic components of a medication. The problem stems from:

- Not consulting the patient's chart for the history of allergies before a new medication is ordered or given
- Not checking a reference to find out if a medication being ordered or given contains any generic components to which the patient has a known allergy

For example, if a patient has an allergy to aspirin, do not administer the first dose of any new medication to the patient without finding out if the product contains aspirin. Although the physician is in error for ordering the medication, you are also in error for administering a medication with which you are unfamiliar. A proficient health care professional should check the history and chart for known allergies and pick up any discrepancies. Alertness is the key to safety in any setting.

According to the Institute for Safe Medication Practices (ISMP) and the FDA, look-alike and sound-alike medications are a leading cause of drug errors. For example, the drug clonidine used for high blood pressure can be confused with the drug clonazepam used for anxiety; Celebrex for arthritis can be confused with Celexa for depression. To help health care professionals differentiate between look-alike and sound-alike drugs, **Tall Man Lettering** is often used to highlight the differences between the two drugs. For example, whereas Celexa would be written CeleXA, Celebrex would be written CeleBREX. This ensures that the health care professional reads and recognizes the correct medication.

These two agencies have created a long-standing relationship with the goal of preventing drug errors. The ISMP has developed tools such as the "List of Confused Drug Names" as a quick drug reference that is available on its website at https://www.ismp.org.

Always keep a drug reference handy and use it when you are unfamiliar with the generic components of a drug ordered for a patient with known drug allergies. For example, a patient reports an allergy to sulfa medications and the provider has ordered Bactrim (trimethoprim/sulfamethoxazole), which contains a sulfa drug and should be avoided. Additionally, consider the difference between an allergy and an expected side effect or intolerance. For example, antibiotics often cause the patient to experience diarrhea; while this can be uncomfortable, it is an expected side effect/intolerance and not a reason to stop the medication. With experience, the names and side effects of products most commonly used at your facility may become easier to remember.

Legal Terms Referring to Drugs

A drug may be referred to by terms other than its classification, generic name, trade name, chemical name, or official name. The following terms imply the legal accessibility of a drug:

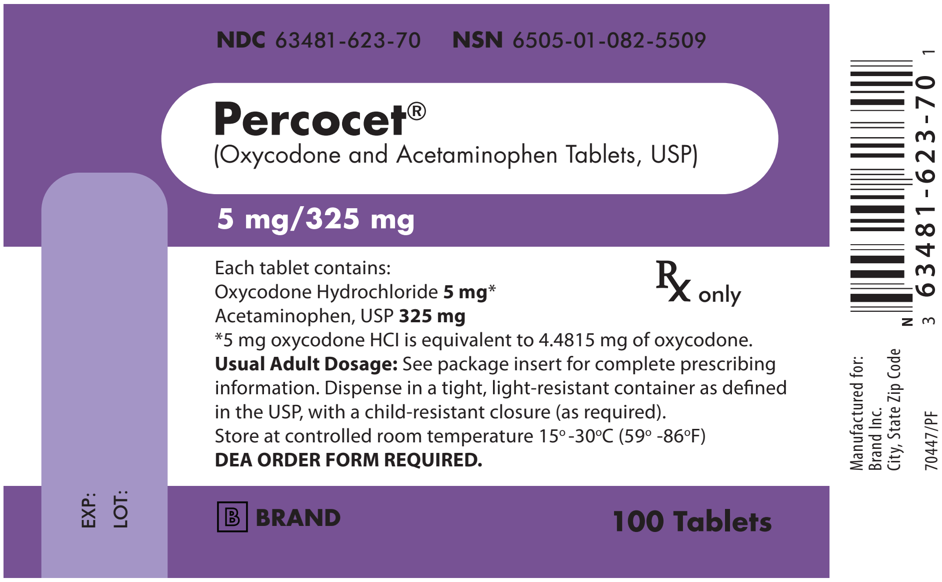
1. ***Over-the-counter (OTC) drug.*** No purchasing restrictions by the FDA (with some exceptions, such as pseudoephedrine, which is OTC, but kept behind the pharmacy counter).
2. ***Legend drug.*** Prescription drug; determined unsafe for OTC purchase because of possible harmful side effects if taken indiscriminately; includes birth control pills, antibiotics, cardiac drugs, and hormones.

3. ***Controlled substance.*** Drug controlled by prescription requirement because of the danger of addiction or abuse; indicated in references by schedule numbers C-I to C-V.
4. ***Off-label medication.*** Drug used in a way not indicated on the FDA label. An example of this would be an antidepressant that is used to treat nerve pain.

In time and with patient research, some prescription drugs can be deemed safe enough to be sold OTC. The OTC Drugs Advisory Committee was formed in 1992 to review prescription or legend drugs and assist the FDA in determining which ones are safe for OTC designation. Some recent examples of previously prescribed medications now available OTC are Nasonex 24HR allergy for nasal allergies and Narcan (naloxone) for suspected opioid overdose, which were approved in 2022 and 2023, respectively.

The legend drug is so named because it requires a legend or warning statement that says, "Federal law prohibits dispensing without a prescription."

Figure 2-1 shows the information contained on a drug label, including the trade name (Percocet) and the generic names of the two drugs (oxycodone and acetaminophen) that it contains. In addition, can you find the controlled substance marking?



NDC 63481-623-70 **NSN** 6505-01-082-5509

Percocet®
(Oxycodone and Acetaminophen Tablets, USP)

5 mg/325 mg

Each tablet contains:
Oxycodone Hydrochloride **5 mg***
Acetaminophen, USP **325 mg**
*5 mg oxycodone HCl is equivalent to 4.4815 mg of oxycodone.
Usual Adult Dosage: See package insert for complete prescribing information. Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).
Store at controlled room temperature 15°-30°C (59°-86°F)
DEA ORDER FORM REQUIRED.

℞ only

EXP:
LOT:

BRAND

100 Tablets

Manufactured for:
Brand Inc.
City, State Zip Code

70447/PF

N 3 63481-623-70 1

Figure 2-1 Information contained on a drug label, including the trade name (Percocet) and the generic names of the two drugs (oxycodone and acetaminophen) that it contains.

Terms Indicating Drug Actions

Most references follow a similar format in describing drugs. When you research drug information, the following terms appear as headings under each drug. Specific information can be found more quickly if you understand what is listed under each heading.

Indications. A list of medical conditions or diseases for which the drug is meant to be used (e.g., the drug diphenhydramine hydrochloride [Benadryl] is indicated to treat allergic rhinitis, mild allergic skin reactions, motion sickness, and mild cases of Parkinsonism).

Actions. A description of the cellular changes that occur as a result of the drug. This information tends to be very technical, describing cellular and tissue changes. Although it is helpful to know what body system is affected by the drug, this information is geared more for the pharmacist (e.g., as an antihistamine, Benadryl appears to compete with histamine for cell receptor sites on effector cells).

Contraindications. A list of conditions for which the drug should *not* be given (e.g., two common contraindications for Benadryl are breastfeeding and hypersensitivity).

Cautions. A list of conditions or types of patients that warrant closer observation for specific side effects when given the drug (e.g., due to atropine-like activity, Benadryl must be used cautiously with patients who have a history of bronchial asthma or glaucoma, or with older adults).

Side effects** and **adverse reactions. A list of possible unpleasant or dangerous secondary effects, other than the desired effect (e.g., side effects of Benadryl include sedation, dizziness, disturbed coordination, epigastric distress, anorexia, and thickening of bronchial secretions). This listing may be quite extensive, with as many as 50 or more side effects for one drug. Because it is difficult to know which are most likely to occur, choose a reference that highlights the most common side effects. Certain drugs may have side effects with which you are not familiar. Note the definitions of the following three side effects associated with specific antibiotics.

- Ototoxicity causes damage to the eighth cranial nerve, resulting in impaired hearing or ringing in the ears (tinnitus). Damage may be reversible or permanent.
- Nephrotoxicity causes damage to the kidneys, resulting in impaired kidney function, decreased urinary output, and renal failure.
- Photosensitivity is an increased reaction to sunlight, with the danger of intense sunburn.

Interactions. A list of other drugs or foods that may alter the effect of the drug and usually should not be given during the same course of therapy (e.g., monoamine oxidase [MAO] inhibitors will intensify the effects of Benadryl; MAO inhibitors will be listed under interactions for many drugs; the term refers to a group of drugs that have been used for the treatment of depression; it has been found that they can cause serious blood pressure changes, and even death, when taken with many other drugs and some foods).

Other headings often listed under information about a drug include “How Supplied” and “Usual Dosage.” “How Supplied” lists the available forms and strengths of the drug. "Usual Dosage" lists the amount of drug considered safe for administration, the route, and the frequency of administration. For example:

How supplied: tablets (tabs): 20 mg and 40 mg; suppository: 20 mg

Usual dosage: 10 mg orally every four hours (q4h)

Clinical Application

While side effects are often negative and cause other issues, sometimes side effects can be beneficial. A side effect is an unintended secondary effect of a drug and in some cases can be good. For example, the medication Proscar is used to treat an enlarged prostate gland, a condition known as benign prostatic hyperplasia (BPH). The active ingredient in Proscar is finasteride, which promotes hair growth. So in a patient with BPH and hair loss, the side effect of increased hair growth might be welcomed! Keep in mind that *adverse reactions* are always bad!

Drug References

The *Physicians' Desk Reference (PDR)* is one of the most widely used references for drugs. It is available online, as a mobile app, and in book form. There are three versions of the *PDR*—one for physicians, one for nurses, and one for consumers. The *PDR* contains full-color photographs of the various drugs, which can aid in identification of unknown medications. You must find the reference most suitable for you, one that you can interpret quickly and easily. By becoming knowledgeable about the drugs administered to patients, you may prevent possible drug errors from occurring.

Other references (e.g., *The Pill Book, Handbook of Nonprescription Drugs*) may be found in bookstores, but they may not contain information adequate for health care professionals. Your school may recommend a specific drug reference other than the three listed in this text. Many new references geared to the nurse or health care professional are currently being made available. Electronic drug references such as Lexi-Drugs, Micromedex, or Epocrates are also widely used. There are applications available for smartphones, and many electronic medication administration records (EMARs) are connected directly to an electronic drug reference.

The Internet as Reference

The Internet offers a wealth of information regarding medications and the conditions they treat. However, there can be serious dangers associated with some online sources that may not be reliable, professional, or even legitimate. Therefore, care must be taken to identify and use only websites that are supervised and controlled, such as those under the auspices of government agencies or sponsored by professional pharmacist groups. It is important for the health care professional to obtain accurate information and also be able to direct the patient or client to reliable sources of information regarding medicines. It is the health care professional's responsibility to caution the layperson regarding the controversial and dangerous practices of "online prescribing" without ever evaluating the patient in person or obtaining medicines without prescriptions through the Internet.

Evaluating Internet Drug Sources

Remember that all websites are not created equal. Pay attention to a few simple rules when seeking the most reputable ones.

1. Check the source. Have scientific studies been done with a large enough sample? Are results reliable and valid? Are there links to a page listing professional credentials or affiliations?
2. Check the date of articles. Medicine is a rapidly evolving field. Information can go out of date quickly.
3. Be wary of information from forums and testimonials. Motivations are unknown. The information is not necessarily valid, and there may be a hidden agenda.

The following websites are reliable professional sources of medical information:

https://www.pharmacist.com	The American Pharmacists Association (APhA), the national professional society of pharmacists.
https://www.fda.gov	U.S. Food and Drug Administration. Includes "Human Drugs" and Center for Drug Evaluation and Research (CDER).
https://www.safemedication.com	SafeMedication.com, developed by the American Society of Health-System Pharmacists. Covers correct dosage, side effects, and optimal use of most prescriptions and OTC drugs. Also offers reports on topics such as antibiotic-resistant bacteria.
https://www.cdc.gov/vaccines/	Centers for Disease Control and Prevention, National Immunization Program. Covers vaccines and immunizations.
http://www.nlm.nih.gov/medlineplus/	MedlinePlus, a service of the National Library of Medicine (NLM) which is part of the National Institutes of Health (NIH). A great source for medicine and related health topics.

Chapter Review Quiz

Match the definition with the term.

1. ____ List of conditions for which a drug is meant to be used
2. ____ Subcategories of drugs based on their effects on the body
3. ____ Description of the cellular changes that occur as a result of a drug
4. ____ Conditions for which a drug should not be given

a. Contraindications
b. Cautions
c. Indications
d. Prototype
e. Actions
f. Classifications

Refer to the following drug description to answer questions 5–8.

AZO Standard®
(phenazopyridine HCl tablets, *USP*)
Product of i-Health, a Division of DSM
Description: AZO Standard (phenazopyridine HCl) is a urinary tract analgesic agent, chemically designated 2,6-pyridinediamine, 3-(phenylazo), monohydrochloride.

5. The generic name of the drug is ____________________

6. The chemical name of the drug is ____________________

7. The trade name of the drug is ____________________

8. What is indicated by the ® symbol after the drug name? ____________________

____

9. Explain when Tall Man Lettering should be used. ____________________

____

10. Explain the difference between these two medication orders:

a. Give two Tylenol, PO.
b. Give one Tylenol No. 2 PO.

____

____

11. An older adult was found unconscious in their bedroom with several pink and blue pills beside their bed, but no labeled pill bottle can be found. They are rushed to the emergency department for treatment. What drug reference source will be most helpful in this situation?

12. Place the following terms in the correct blank: OTC, controlled substance, legend drug, off-label drug

a. __________ a prescription is *not* needed
b. __________ term that means a prescription is required
c. __________ potential for abuse
d. __________ drug given for an unapproved use

Chapter 3

Sources and Bodily Effects of Drugs

Key Terms and Concepts

Adverse drug reaction
Anaphylactic reaction
Chemoinformatics
Cumulative effect
Dependence
Dosage
Drug interactions
Drug processes
Hypersensitivity
Idiosyncratic reaction
Keep Vein Open (KVO)
Local effect
Paradoxical reaction
Pharmacogenomics
Placebo effect
Prodrugs
Sources of drugs
Systemic effect
Teratogenic effect
Therapeutic range
Tolerance

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify the five sources of drugs.
2. Contrast systemic and local effects.
3. Define the pharmacokinetic processes as they relate to the passage of drugs through the body.
4. State conditions that may decrease the effectiveness of each pharmacokinetic process: absorption, distribution, metabolism, and excretion.
5. List several variables that can affect drug action.
6. Define various adverse drug reactions.
7. Describe the various routes of drug administration.

Sources of Drugs

Any chemical substance ingested or applied on the body for the purpose of affecting body function is referred to as a drug. In earlier times, these substances were found in nature, sometimes accidentally. Plants were the primary **sources of drugs** used on the human body. Substances contained in berries, bark, leaves, resin from trees, and roots were found to aid the body, and these are still very important drug sources.

Minerals from the earth also found their way into human use as drugs. Minerals such as iron, sulfur, potassium, silver, and even gold are used to manufacture drugs.

More sophisticated sources of drugs have emerged as human beings have progressed. Research led to the use of substances from *animals* as effective drugs. Substances lacking in the human body can be replaced with similar substances obtained from the glands, organs, and tissues of animals. Investigation of other animal sources of medicines still remains. For example, an investigational drug to treat type 2 diabetes by promoting weight loss was recently developed from the saliva of the Gila monster lizard.

Chemists use synthetic sources to make drugs to market for human consumption. The *synthetic* (manufactured) sources have evolved with human skills in laboratories and advanced understanding of chemistry. Today, through advances in computers, millions of potential drug candidates can be screened on computers quickly and efficiently using a process called chemoinformatics. **Chemoinformatics** is the application of computer technology, statistics, and mathematics to study information about the structure, properties, and activities of molecules. This method is probably the most actively pursued source of drugs by major companies today. Competitive research is a big industry that involves experimenting with chemicals to discover cures for current medical problems. Numerous antibiotics are synthetic or semisynthetic, the results of researchers meeting the need for better treatment of infections. Someday the cure for cancer or human immunodeficiency virus (HIV) infection may be found from a synthetic source developed in a laboratory.

Genetic engineering of drugs and the technique of *recombinant DNA technology* has allowed for the production of biologically active substances that are present in the body and that can be used to treat certain diseases. DNA is the genetic material of the cells, and the DNA sequence determines the genetic code. Genetic engineering refers to the alteration of genes in a laboratory setting.

Recombinant DNA techniques involve combining the DNA of two or more different organisms for a desired change or improvement. Some examples of therapeutic agents derived from recombinant DNA technology are the hepatitis B vaccine, insulin, and growth hormone. One of the areas of most current interest in recombinant DNA technology is gene therapy. This therapy consists of essentially inserting normal genes into a human chromosome to counteract the effects of an abnormal or a missing gene. This has not only huge implications for preventive medical therapy but also ethical considerations. Figure 3-1 lists examples of sources of drugs.

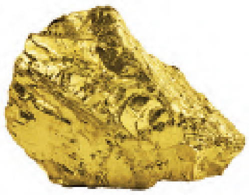
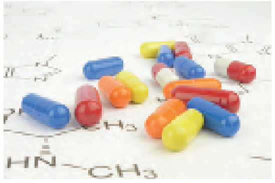
Sources of Drugs	Example	Trade Name	Classification
Plants Foxglove where digitalis was originally found Picture Partners/Shutterstock.com.	Cinchona Bark Purple Foxglove Plant Poppy Plant (Opium)	Quinidine Digitalis Morphine, Codeine	Antiarrhythmic Cardiotonic Analgesic Analgesic, Antitussive
 Minerals macrowildlife/Shutterstock.com.	Magnesium Zinc Gold	Milk of Magnesia Zinc Oxide Ointment Auranofin	Antacid, Laxative Sunscreen, Skin Protectant Anti-inflammatory; Used in the Treatment of Rheumatoid Arthritis
Animals sal73it/Shutterstock.com.	Thyroid Gland of Animals	Thyroid, USP	Hormone
 Synthetic Vadim.Petrov/Shutterstock.com.	meperidine diphenoxylate co-trimoxazole	Demerol Lomotil Bactrim, Septra	Analgesic Antidiarrheal Anti-infective Sulfonamide; Used in the Treatment of Urinary Tract Infections (UTI) and some other Infections
DNA Genetic Engineered metamorworks/Shutterstock.com.	Hepatitis B vaccine Insulin Growth hormone	Recombivax HB Humulin, Novolin Nutropin	Vaccine Anti-diabetic Hormone

Figure 3-1 Sources of drugs: plants, minerals, animals, synthetic, and genetically engineered.

Effects of Drugs

Regardless of the source, the common characteristic all drugs share is the ability to affect body function in some manner. When introduced into the body, all drugs cause cellular changes (drug actions), followed by some *physiological change* (effects of drugs). Generally, drug effects may be categorized as systemic or local:

1. **Systemic effect.** Reaches widespread areas of the body. For example, ibuprofen is often used as an analgesic and anti-inflammatory for pain associated with knee pain due to arthritis. Although you feel the effect in your knee, the medication is actually providing the same effect all over the body, which is why it can also be used for headaches, cramps, and sunburn just to name a few. Systemic effects are widespread because the medication reaches the bloodstream and is carried throughout the body.
2. **Local effect.** Is limited to the area of the body where it is administered (e.g., dibucaine ointment [Nupercainal], applied rectally, affects only the rectal mucosa to reduce hemorrhoidal pain). Many topical skin creams such as those used to treat pimples only work locally where they are applied and needed. Most medications taken by mouth have systemic effects, with exceptions being with medications that affect the inner mucosal layer of the stomach.

Drug Processing by the Body (Pharmacokinetics)

***Kinetics* means "movement" and therefore *pharmacokinetics* literally means what happens to the drug as it moves through our body.**

Within the body, drugs undergo several changes. From start to finish, the biological changes consist of four **drug processes** (abbreviated as *ADME*):

1. ***Absorption.*** Passage of a substance through a membrane into the bloodstream
2. ***Distribution.*** Moving from the bloodstream into the tissues and fluids of the body
3. ***Metabolism.*** Physical and chemical alterations that the substance undergoes in the body
4. ***Excretion.*** Eliminating waste products of drug metabolism from the body

Many variables affect how quickly or successfully substances go through the body via these four processes. If any of the four processes are altered, the drug action and effects will be altered, where the medication may have a greater or lesser effect or a longer or shorter duration. Table 3-1 lists conditions that may alter each process.

Directions for the administration of drugs may vary widely because the physical properties of the drugs vary widely. The specific directions ("Usual Dosage and

Table 3-1 Processing of Drugs within the Body

Process	Primary Site of Process	Conditions That May Alter Process
Absorption	Mucosa of the stomach, mouth, small intestine, or rectum; blood vessels in the muscles or subcutaneous tissues; or dermal layers	Incorrect administration may destroy the drug before it reaches the bloodstream or its site of action (e.g., giving certain antibiotics after meals instead of on an empty stomach)
Distribution	Circulatory system, through capillaries and across cell membranes	Poor circulation (impaired flow of blood) may prevent the drug from reaching tissues where it is to have its desired effect.
Metabolism	Liver, small intestine	Hepatitis, cirrhosis of the liver, or a damaged liver may prevent adequate breakdown of the drug, thus causing a build-up or accumulation of unmetabolized drug.
Excretion	Kidneys, sweat glands, lungs, or intestines	Renal damage or kidney failure may prevent passage of drug waste products, thereby causing an accumulation of the drug in the body

Administration," "Contraindications," and "Warnings") that accompany each drug are given to enhance the absorption, distribution, metabolism, and excretion of the drug. For example, directions to "Give on an empty stomach" ensure the most effective means of absorption. "Use cautiously in patients with renal dysfunction" implies possible effects on the excretion of a drug. "Decrease dose in patients with hepatic dysfunction" implies possible effects on the metabolism of a drug. *Read all labels carefully and caution the patient to do so as well* (Figure 3-2).

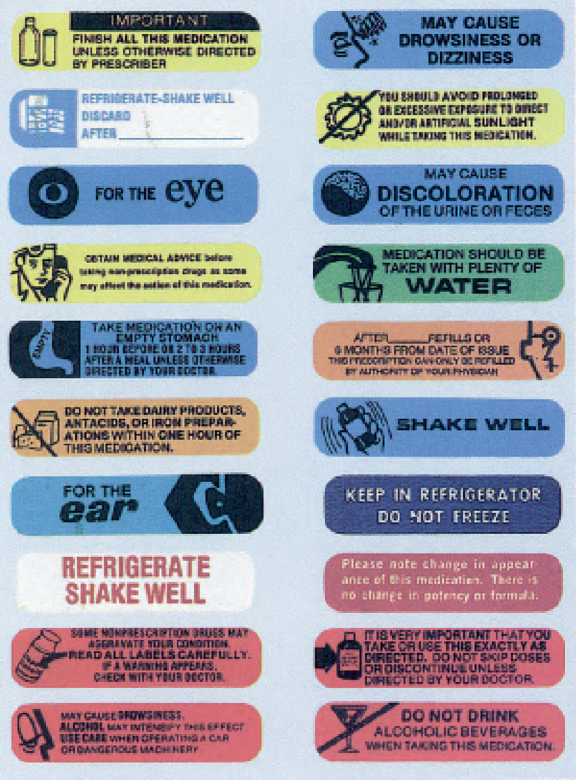

IMPORTANT
FINISH ALL THIS MEDICATION UNLESS OTHERWISE DIRECTED BY PRESCRIBER
MAY CAUSE DROWSINESS OR DIZZINESS
REFRIGERATE-SHAKE WELL
DISCARD
AFTER
YOU SHOULD AVOID PROLONGED OR EXCESSIVE EXPOSURE TO DIRECT AND/OR ARTIFICIAL SUNLIGHT WHILE TAKING THIS MEDICATION.
FOR THE eye
MAY CAUSE
DISCOLORATION
OF THE URINE OR FECES
OBTAIN MEDICAL ADVICE before taking non-prescription drugs as some may affect the action of this medication.
MEDICATION SHOULD BE TAKEN WITH PLENTY OF WATER
TAKE MEDICATION ON AN EMPTY STOMACH
1 HOUR BEFORE OR 2 TO 3 HOURS AFTER A MEAL UNLESS OTHERWISE DIRECTED BY YOUR DOCTOR.
AFTER ____ REFILLS OR 6 MONTHS FROM DATE OF ISSUE THIS PRESCRIPTION CAN ONLY BE REFILLED BY AUTHORITY OF YOUR PHYSICIAN
DO NOT TAKE DAIRY PRODUCTS, ANTACIDS, OR IRON PREPARATIONS WITHIN ONE HOUR OF THIS MEDICATION.
SHAKE WELL
FOR THE ear
KEEP IN REFRIGERATOR
DO NOT FREEZE
REFRIGERATE
SHAKE WELL
Please note change in appearance of this medication. There is no change in potency or formula.
SOME NONPRESCRIPTION DRUGS MAY AGGRAVATE YOUR CONDITION.
READ ALL LABELS CAREFULLY.
IF A WARNING APPEARS, CHECK WITH YOUR DOCTOR.
IT IS VERY IMPORTANT THAT YOU TAKE OR USE THIS EXACTLY AS DIRECTED. DO NOT SKIP DOSES OR DISCONTINUE UNLESS DIRECTED BY YOUR DOCTOR.
MAY CAUSE DROWSINESS.
ALCOHOL MAY INTENSIFY THIS EFFECT
USE CARE WHEN OPERATING A CAR OR DANGEROUS MACHINERY
DO NOT DRINK
ALCOHOLIC BEVERAGES
WHEN TAKING THIS MEDICATION.

Figure 3-2 Warning labels are placed on prescription medication containers. Patients should be advised to read and follow these precautions or instructions.

Absorption

The site of absorption of drugs varies according to the following physical properties of each drug:

1. ***pH.*** Drugs of a slightly acidic nature (e.g., aspirin and tetracycline) are absorbed well within the acidic stomach environment. Drugs of an alkaline pH are not absorbed well through the stomach but are readily absorbed in the alkaline environment of the small intestine. The antibiotic tetracycline is not recommended to be administered with milk, dairy products, or antacids because it will not be properly absorbed. This is due to *chelation*—the formation of an insoluble complex of tetracycline with calcium in dairy products. pH effect may also play a role. Oral medications for infants (syrups and solutions) may not be absorbed well after infant feedings. The milk or formula neutralizes the acidity of the stomach. Thus, absorption may be enhanced when the infant is given medications on an empty stomach.
2. ***Lipid (fat) solubility.*** Substances high in lipid solubility are quickly and easily absorbed through the mucosa of the stomach. Alcohol and substances containing alcohol are soluble in lipids. They are rapidly absorbed through the gastrointestinal (GI) tract. Substances low in lipid solubility are not absorbed well through the stomach or intestinal mucosa and are absorbed best when given by a means other than the GI tract. An exception is the drug neomycin, which is not lipid soluble and yet is given orally. It is indicated for suppression of intestinal bacteria before intestinal or bowel surgery or for the treatment of bacterial diarrhea. By giving neomycin orally, it passes through the GI tract, unable to be absorbed. As a result, it tends to build up and accumulate in the bowel. The trapped antibiotic kills the bacteria in the bowel, achieving the desired effect.
3. ***Presence or absence of food in the stomach.*** Food in the stomach tends to slow absorption due to a slower emptying of the stomach. If a fast drug effect is desired, an empty stomach will facilitate quicker absorption. On the other hand, giving some medications on an empty stomach is contraindicated. Medications that are irritating to the stomach can be buffered by the presence of food. Directions may indicate "Give after meals" or "Take with food" to decrease side effects (e.g., nausea and gastric ulcers) in the GI tract.

Distribution

The movement of a drug from the bloodstream into the tissues and fluids of the body is also affected by specific properties of the drug. Reaching sites beyond the major organs may depend on the drug's ability to cross a lipid membrane. Whereas some drugs pass the "blood–brain barrier" to reach the brain or the "placental barrier" to reach the developing fetus, others do not. For example, propranolol is the only beta-blockers (normally a cardiac medication) that passes the blood–brain barrier, and this allows it to be used for an adjunct therapy for migraine headaches because it can have an effect in the brain. You may also read about drugs that are contraindicated for lactating mothers because the drug has the ability to pass through cell membranes into the milk.

Some drugs have a *selective distribution*. This refers to an affinity, or attraction, of a drug to a specific organ or cell. For example, amphetamines have a selective distribution to cerebrospinal fluid. The human chorionic gonadotropin hormone, which is used as a fertility drug, has a selective distribution to the ovaries.

By virtue of their properties, some drugs are distributed more slowly than others. Thus, although two drugs may be categorized in the same drug classification, one may be known to act on the cells and achieve the effect more quickly than the other.

Metabolism

When transformed in the liver (biotransformation), a drug is broken down and altered to more water-soluble by-products (metabolites). Thus, the drug may be more easily excreted by the kidneys. Some drugs are inactive when administered and become active only when they are metabolized by the liver. This group of drugs is known as **prodrugs** (e.g., clopidogrel [Plavix]).

If hepatic disease is present, a patient may exhibit toxic (poisonous) effects of a drug, or the drug may not work as intended. This occurs because the drug is not being broken down properly by the inefficient liver. The drug may accumulate, unchanged by the liver, and may be unable to pass out of the body's excretory system. Metabolism can also be altered by interactions between drugs, between drugs and food, and between drugs and disease states. For example, as mentioned previously, clopidogrel is a prodrug, but its metabolism to the active form is inhibited by Nexium (esomeprazole). If these drugs are used together, clopidogrel will not have its intended antiplatelet effect.

It is possible for some drugs to bypass the process of metabolism. They reach the kidneys virtually unchanged and may later be detected in the urine.

Excretion

Although it is possible for some drugs to be eliminated through the lungs (e.g., exhaled gases and anesthetics) or through perspiration, feces, bile, or breast milk, most are excreted by the kidneys in the urine.

If a drug is not excreted properly before repeated doses are given, a cumulative effect due to a drug build-up may eventually occur. A **cumulative effect** is an increased effect of a drug demonstrated when repeated doses accumulate in the body. Patients with decreased kidney function may be at risk of drug accumulation. If unnoticed, the cumulative effect may build to a dangerous, or toxic, level. This can be of particular concern with older adults.

Toxicity refers to a condition that results from exposure to either a poison or a dangerous amount of a drug that is normally safe when given in a smaller amount. In drug therapy, the goal is to give just enough of the drug to cause the desired (therapeutic) effect while keeping the amount below the level at which toxic effects are observed. It should be noted that toxicity can develop even with properly dosed or small amounts of a drug.

Digoxin is a cardiac drug that must be given cautiously because of its potential for causing a cumulative effect. Normally, digoxin slows the heart rate, but if the drug accumulates, the heart rate may slow to a dangerously low level. Circulation and renal function must be adequate, or the digoxin will accumulate, leading to digoxin toxicity.

Keep in mind that the purpose of most medication treatment is to have a desired effect by maintaining a drug level within a therapeutic range. The **therapeutic range** is the range of drug levels in the blood that will give the desired effect without causing serious side effects. The blood can be tested for therapeutic levels. For example, the target therapeutic range for digoxin is 0.8–2.0 ng/mL. Levels lower than this will not be effective, and levels higher than this range can lead to toxicity.

Other Variables Affecting Drug Action

Many *variables* affect the speed and efficiency of drugs being processed by the body. The physical properties of the drugs themselves and the condition of the body systems have been discussed. Other variables affecting drug action and effect follow.

Age

Metabolism and excretion are slower in older adults, and therefore attention must be paid to possible cumulative effects. Children have a lower threshold of response and react more rapidly and sometimes in unexpected ways; therefore, frequent assessment is imperative.

Weight

Generally, the bigger the person, the greater the dose should be. However, there is great individual variation in sensitivity to drugs. Many drug dosages are always calculated on the basis of the patient's weight. With certain drugs in patients who are obese, it may be best to calculate their dose based on their ideal body weight rather than their total body weight.

Sex

Females respond differently than males to some drugs. The ratio of fat per body mass differs, and so do hormone levels. Drugs should be selected carefully for individuals who may be pregnant or nursing. For example, the common over-the-counter medications ibuprofen and naproxen (Advil and Aleve) should never be used during pregnancy unless under medical supervision.

Psychological State

It has been proven that the more positive the patient's feelings about the medication being taken, the more positive the patient's physical response will be. This is referred to as the **placebo effect**.

A *placebo* is an inactive substance that resembles a medication, although no drug is present. For example, a sugar tablet or a saline solution for injection may be used as a placebo in a research study program.

Placebos are most often used in blind study experiments in which groups of people are given either a drug or a placebo. (Needless to say, placebos are not administered if doing so would risk serious or irreversible harm to those taking them.) The individuals, unaware of which they have been given, are studied for the effects. Often, by virtue of strong belief or by the natural fluctuation of a disease (e.g., headaches may get better without treatment), the placebo-administered individuals achieve the desired effect associated with the drug they think they have received.

It is also possible for a drug's effect to decrease when the attitude of a patient toward a medication is negative. Attitudes toward medicines can also be influenced positively or negatively by cultural or religious beliefs. The caregiver needs to understand the importance of these beliefs to the patient.

The significance of the placebo effect for you, the health care professional, is to recognize that your attitude regarding a medication may be picked up by the patient and indirectly may affect the patient's response to the drug.

Drug Interactions

Often patients are prescribed multiple drugs. Whenever more than one drug is taken, it is possible that the *combination* may alter the normal expected response of each individual drug, a phenomenon known as **drug interactions**. One drug may interact with another to increase, decrease, or cancel out the effects of the other.

The following terms are used to describe drug interactions:

Synergism. The action of two drugs working together in which one helps the other simultaneously for an effect that neither could produce alone. Drugs that work together are said to be synergistic.

Potentiation. The action of two drugs in which one prolongs or multiplies the effect of the other. Drug A may be said to potentiate the effect of drug B. This interaction is often used in pain medications.

Antagonism. The opposing action of two drugs in which one decreases or cancels out the effect of the other. Drug A may be referred to as an antagonist of drug B.

To prevent undesirable drug interactions, it is extremely important for the prescribing physician to know of all medications that a patient is taking. On the other hand, it may be intentionally ordered that two drugs be taken together because some drug interactions are desirable and beneficial. Compare the following situations, keeping in mind that any of the situations described can be desirable or undesirable based on the drugs and their effects.

Synergism. Simvastatin (Zocor) (lowers high cholesterol) and gemfibrozil (Lopid) (lowers high triglycerides) are very effective in treating patients who have both high cholesterol and triglyceride levels (collectively called high lipids). By giving small amounts of each together, high lipid levels can be treated more effectively. On the other hand, opioid analgesics and benzodiazepines can both cause sedation and drowsiness; when taken together this effect can become severe. To put this in terms of simple numbers, $1 + 1 = 3$, meaning the effect of both drugs together is more than that of each when given separately; both drugs are contributing to the amount of the effect.

Potentiation. To build up a high level of some forms of penicillin (an antibiotic) in the blood, the drug probenecid (antigout medication) can be given simultaneously. Probenecid potentiates the effect of penicillin by slowing the excretion rate of the antibiotic. To put this in terms of simple numbers, $1 + 0 = 2$, meaning the effect of one drug is increased due to being given with the other, even though the second drug does not contribute to the observed effect.

Antagonism. A narcotic antagonist (e.g., naloxone [Narcan]) saves lives from drug overdoses by reversing the clinical effect of narcotics. On the other hand, antacids taken at the same time as tetracycline may alter the pH or form chelates, which are insoluble complexes that prevent the absorption of tetracycline.

To put this in terms of simple math, 1 + 1 = 0, meaning that the effect of one drug lowers or eliminates the effects of the other.

Dosage

Different dosages of a drug may bring about variations in the speed of drug action or effectiveness. **Dosage** is defined as the amount of a drug given for a particular therapeutic or desired effect. Terms of various dosage levels are:

1. ***Minimum dose.*** Smallest amount of a drug that will produce a therapeutic effect.
2. ***Maximum dose.*** Largest amount of a drug that will produce a desired effect without producing symptoms of toxicity.
3. ***Loading dose.*** Initial high dose (often maximum dose) used to quickly elevate the level of a drug in the blood (often followed by a series of lower maintenance doses).
4. ***Maintenance dose.*** Dose required to keep the level of a drug in the blood at a steady state to maintain the desired effect.
5. ***Toxic dose.*** Amount of a drug that will produce harmful side effects or symptoms of poisoning.
6. ***Lethal dose.*** Dose that causes death.
7. ***Therapeutic dose.*** Dose that is customarily given (average adult dose based on body weight of 150 lb); adjusted according to variations from the norm.

You may be familiar with the use of a high loading dose followed by a lesser maintenance dose. If you have taken antibiotics, you may have been instructed to take two tablets or capsules initially and then to take one tablet every six hours. It is frequently desirable to give a loading dose of antibiotics to quickly build up a high level of the drug in the blood initially and get the process of killing the bacteria started.

Pharmacogenomics

Did you know that for certain groups of medications the chance of achieving the desired effect is only around 30 to 60 percent? This rather dismal response rate may be due to an individual's genetic background. The science that examines how our genes may explain if a drug should work and if it will be toxic to our bodies is known as **pharmacogenomics**. For example, the enzymes that metabolize drugs are genetically determined. Because of this, some of us may metabolize drugs more quickly or more slowly than the average person. This may cause the drug to have a greater effect in a slow or poor metabolizer and possibly a poor effect (or no effect) in a rapid metabolizer compared to the average person. The hope is that the science of pharmacogenomics will help optimize drug therapy in individual patients by increasing effectiveness, reducing toxicity, and avoiding unnecessary treatment.

Clinical Connection

Because of a high rate of overdoses from both prescription narcotics and illegal opioids such as heroin and fentanyl, the opioid antagonist naloxone (Narcan) is used by prescribers to ensure patients and families are prepared in the case of an overdose. According to the National Institute on Drug Abuse, over 70,000 Americans died from overdose involving synthetic opioids (primarily fentanyl) in 2021. Naloxone works to quickly reverse the effects of opioids by using antagonism at the receptors where the drug is located. It can be administered via injection or nasal inhalation and will revive a person who has stopped breathing due to an overdose. Naloxone is available over the counter or by prescription.

Before we dive into a further discussion of pharmacogenomics, it is important to understand some basic genetic information. Genes are a piece of DNA (deoxyribonucleic acid) that contains instructions for making proteins. Proteins perform cellular functions. Some genes do not code for proteins but regulate the activity of other genes that do. These genes reside on chromosomes. Chromosomes are structural units for organizing DNA. Humans normally have 23 pairs of chromosomes (46 chromosomes total).

The basic building blocks of DNA are called nucleotides. There are four nucleotides: adenine (A), guanine (G), thymine (T), and cytosine (C). Polymorphisms are variations in the DNA sequence that may involve one nucleotide change (single nucleotide polymorphism or SNP, pronounced "snip") or the addition or deletion of an entire gene. These polymorphisms may affect drug pharmacokinetics or pharmacodynamics.

Now we will use a few examples to illustrate how pharmacogenomics may improve patient care. Mercaptopurine is a medication that is used to treat acute lymphoblastic leukemia (a blood cell cancer). It is metabolized by an enzyme abbreviated TMPT. Polymorphisms of this enzyme exist, and some people are poor metabolizers of mercaptopurine. A genetic screening test may be ordered prior to giving a patient this medicine. If the patient is found to be a poor metabolizer, the dose of mercaptopurine will be reduced to avoid drug accumulation and increased bone marrow toxic effects (causes red and white blood cells and platelets to be reduced).

CYP2DG is an enzyme found in the liver that is responsible for metabolizing quite a few drugs. Depending on an individual's genetic makeup, they may have enzyme activity that causes their ability to metabolize drugs to range from poor to highly active. The Food and Drug Administration (FDA) has issued a warning to health care professionals concerning serious adverse effects of normal doses of codeine, including death in children, on individuals with particular genetic anomalies following the deaths of three children who died after receiving normal dosages of codeine after having their tonsils removed. Three children who died had a genetic variation in their CYP2DG enzyme, which caused the codeine to be rapidly metabolized to morphine, possibly leading to an overdose and death. Medications that may be affected by genetic variations in the CYP2DG gene include antidepressants, beta-blockers, and tamoxifen, as well as many others.

By now you may be wondering why we do not use pharmacogenomic information more frequently. There are ethical issues to consider such as loss of privacy, genetic profiling, and the potential for discrimination. More research is necessary to prove that pharmacogenomics improves patient outcomes. Table 3-2 lists some examples of pharmacogenomic tests.

Routes of Administration

The route of administration is probably the most significant factor in the speed of drug action.

The route of drug administration can be compared to the route of travel. In planning a trip from point A to point B, you may have a map that shows several courses of travel to reach the destination. The course you select is optional, depending on your choice for the quickest, cheapest, safest, or most scenic route.

Table 3-2 Examples of Pharmacogenomic Laboratory Tests

Drug	Test	Specimen	Clinical Use
warfarin	VKORC1, CYP2C9	Blood, buccal swab	Aids in determining proper dosage
abacavir	HLA-B 5701	Blood, buccal swab	Detects chance of hypersensitivity
tamoxifen	CYP2D6	Blood, buccal swab	Determines how fast drug will be metabolized
carbamazepine	HLA-B 1502	Blood, buccal swab	Detects chance of hypersensitivity
azathioprine	TMPT	Blood	Detects chance of toxicity
trastuzumab	HER-2	Biopsy of cancerous tissue	Determines treatment options

Options for routes of drug administration are similar in that there are a number of methods by which drugs may be given to reach their destination. Sometimes, the route selected is based on the degree of speed, cost, ease, or safety of administration. Sometimes, there is no choice of routes because some medications can be given by only one route. Often this is because absorption occurs only by that route, or the substance is dangerous or toxic when given by another route. Insulin, for example, may be given only by injection and via inhalation. Much research has been done to produce an oral form of insulin, but attempts have failed because the drug is destroyed by gastric juices.

The most common routes of administration may be grouped into two main categories as mentioned in the following list:

1. *Enteral or GI tract routes*
   - Oral (PO)
   - Nasogastric tube (NG) and gastric tube
   - Rectal (R) or (PR = per rectum)
2. *Parenteral routes*, which include any route other than the GI tract
   a. Injection routes
      - Intravenous (IV)
      - Intramuscular (IM)
      - Subcutaneous (SQ)
      - Intradermal (ID)
      - Intracardiac, intraosseous, intraspinal, intraventricular, and intracapsular[1]

   b. Nonparenteral routes (standalone routes)
      - Sublingual (SL) (under the tongue) or buccal (cheek: absorbed through mucosa, not swallowed) (*Note:* some classify SL and buccal as oral routes)
      - Transdermal or dermal (D) (skin patches that allow the drug to be slowly absorbed systemically)
      - Topical (T)
      - Ophthalmic (eyes)
      - Otic (ears)

---

[1] *These five injection routes are less common and are administered by the physician.*

- Transvaginal
- Nasal
- Inhalation

The term *enteral* means within, or by way of, the intestine. The term *parenteral* is derived from the Greek term *para*, "apart from," plus *eneteron*, "the intestine." Therefore, *parenteral* technically means any route other than the gastrointestinal (GI) tract. In medical practice, parenteral is usually used to refer to injectables, while the rest of the non-injectable routes are referred to as stand-alone routes.

There are advantages and disadvantages in the use of each route. The physician's choice of a particular route of drug administration may depend on (1) desired effects (e.g., fast or slow, local or systemic), (2) absorption qualities of the drug, and (3) how the drug is supplied. Other general points regarding the effect of the route on drug absorption are as follows:

1. The oral route is the easiest, but the effects are slower because of the time required for dissolution of the drug product in the alimentary canal before absorption.
2. The intravenous (IV) route is the fastest: drugs enter the bloodstream immediately. Doses to be given IV are in small amounts; effects are immediate and can be quite dangerous if given in amounts recommended for other routes. IV drugs can be administered by IV push or bolus (a concentrated drug solution) (Figure 3-3), or they can be diluted, and solutions are then infused more slowly by IV drip.
   a. IVs are administered by a physician, nurse, or paramedic.
   b. IV is the best route for treatment of emergencies because of the speed of action.
   c. IV fluids are used for rehydration and to replace electrolytes.
   d. **Keep Vein Open (KVO)** is a slow rate of IV fluid administration used to maintain the patency of the IV for quick access for medication delivery.

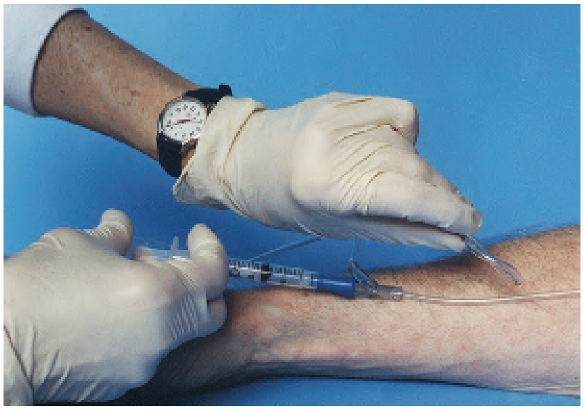


Figure 3-3 Intravenous (IV) push or bolus; IV drugs are administered slowly over a specified period of time (usually one to seven minutes).

3. Parenteral routes are the choice when:
   a. Patient can take nothing by mouth.
   b. The drug is not suitable for GI absorption.
4. The intramuscular route is fairly rapid because the muscles are highly vascular. If it is desirable to slow the speed of absorption, the drug to be given IM may be added to an oily base.
5. The transdermal route allows for slower consistent drug absorption over time, allowing the patient to usually place one patch on in the morning for the entire day.
6. The inhalation route is fast-acting due to the large surface area of the lungs and rich blood supply, which allows the drug to enter the bloodstream quickly. This route often requires more involved patient cooperation, and therefore education, to be effective.

Unexpected Responses to Drugs

Unintended effects from medications are termed *side effects* and can include a host of reactions such as cough, pain, tremors, headaches, dizziness, change in laboratory values, and photosensitivity. They can also be useful: for example, when Benadryl causes drowsiness it can be used as a sleep aid in addition to its normal use as an antihistamine. When side effects cause the patient to have a negative reaction, it is termed an **adverse drug reaction**, and many times a change in drug, dose, or frequency is needed to prevent one. Several other terms must be defined to complete your awareness of the bodily effects of drugs. These terms refer to adverse drug effects.

Teratogenic effect. Effect from maternal drug administration that causes physical defects in a fetus. The FDA requires that medication labels have narratives that discuss the following subsections: Pregnancy (includes labor and delivery), Lactation, and Females and Males of Reproductive Potential. Theses sections provide information to make an informed decision on the safety of these medications.

Idiosyncratic reaction. Unique, unusual, and unexpected response to a drug.

Paradoxical reaction. Opposite effect from that expected. For example, a patient may have a paradoxical reaction to a particular tranquilizer if it causes agitation and excitement rather than tranquility.

Tolerance. Decreased response to a drug that develops after repeated doses are given. To achieve the desired effect, either the drug dosage must be increased or the drug must be replaced.

Dependence. Acquired need for a drug that may produce psychological or physical symptoms of withdrawal when the drug is discontinued.

- Psychological dependence involves only a psychological craving; no physical symptoms of withdrawal are found other than anxiety.
- Physical dependence exists when cells actually have a need for the drug; symptoms of withdrawal include retching, nausea, pain, tremors, and sweating.

Hypersensitivity. Immune response (allergy) to a drug may be of varying degrees.

- May be mild with no immediate effects; rash or hives may appear after three to four days of drug therapy.
- May develop after uneventful previous uses of a drug.
- More likely to exist in patients with other known allergies.

Anaphylactic reaction. Severe, possibly fatal, allergic (hypersensitivity) response.

- Signs include itching, urticaria (hives), hyperemia (reddened, warm skin), vascular collapse, shock, cyanosis, laryngeal edema, and dyspnea (difficulty breathing).
- Treatment includes cardiopulmonary resuscitation (CPR) if indicated and drugs as required: epinephrine (Adrenalin) and fluids to raise blood pressure; corticosteroid (Solu-Medrol) to reduce inflammation and the body's immunological response; or antihistamine (Benadryl) to suppress histamine, thereby reducing redness, itching, and edema.

Learning Hint

Think of adverse drug reactions as the broad term for anything that can go wrong due to being given a drug. An allergy is a type of adverse drug reaction that causes hypersensitivity, which then causes the immune system to go overboard in its response. Nausea, vomiting, and diarrhea are not considered signs of allergies but are actually adverse drug reactions themselves. The allergic response has a range and can be mild and manifest as hives or itchiness, or it can be extreme and become anaphylactic shock with severe loss of blood pressure.

Anaphylaxis has been noted often with the following: antibiotics, especially penicillin; X-ray dyes containing iodides (such as IVP [intravenous pyelogram] dye, angiogram dye, gallbladder dyes, etc.); foods (shellfish, onions, peanuts, etc.); and insect stings (bees and ants).

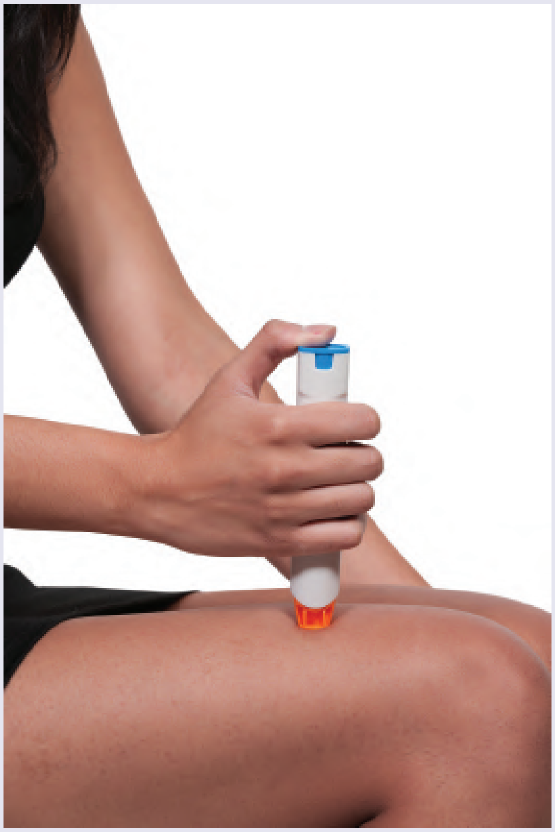
Knowledge of any adverse reactions to drugs should be included in the patient's history. This information can be helpful in preventing repeated episodes. Getting an accurate drug history and clearly listing known allergies is a critical function of the health care professional.

Persons who have had an anaphylactic reaction to a substance should always wear a *Medic-Alert tag* or *bracelet* to identify the substance to which they are extremely allergic. Persons who have had hypersensitivity reactions to a substance are more at risk for reactions to other substances as well. Allergies should be listed on a card and carried in the wallet of the individual who is sensitive.

Extreme caution should be taken when giving a medication, especially antibiotics, to a patient for the first time, particularly if the patient has a history of other allergies.

Clinical Connection

Epi-pens are often provided to patients who have a severe allergy that they may be exposed to unintentionally, such as a bee sting or peanuts in a baked product. It is important to educate the patient, as well as family and friends, on how to properly use the epi-pen in case of an emergency. As shown in Figure 3-4, the epi-pen should be injected in a straight downward direction directly into a large muscle. It should be noted that it can be administered through a normal layer of clothing such as a pair of pants or shirt.



Rob Byron/Shutterstock.com.

Figure 3-4 An epi-pen can be used to treat the severe allergic reaction known as anaphylaxis.

Chapter Review Quiz

Fill in the blanks.

1.

Drug Sources	Example	Trade Name	Classification

2. Drugs that are distributed throughout the body have ______________________________ effects.

3. Drugs whose action is limited to a specific location have ____________________________ effects.

4. As drugs pass through the body, they undergo four processes:

Process	Definition of Process

5. Factors that may affect the passage of drugs through the body:

Process	Primary Site of Process	Conditions Altering Process

6. If circulation is poor, metabolism is faulty, or excretion is inadequate, drugs may build up in the system, leading to ________________ effects, causing poisonous, or ______________________, levels of the drug.

7. Variables affecting the efficiency of drug action include ________, ________, ________, and ________.

Match the term with the definition.

8. Synergism __________

9. Antagonism __________

10. Potentiation __________

11. Lethal dose __________

12. Toxic dose __________

13. Maintenance dose ______

14. Idiosyncrasy __________

15. Tolerance __________

16. Dependence __________

17. Teratogenic __________

a. Amount of drug required to keep drug level steady

b. Amount of drug that can cause death

c. Amount of drug that can cause dangerous side effects

d. One drug making the effect of another drug more powerful

e. Drugs working together for a better effect

f. Drugs working against each other or counteracting each other's effect

g. Acquired need for a drug, with symptoms of withdrawal when discontinued

h. Unusual response to a drug, other than expected effect

i. Effects on a fetus from maternal use of a drug

j. Decreased response after repeated use of a drug, increased dosage required for effect

Fill in the blanks.

18. An allergy or immune response to a drug is called ____

____

19. Allergic reactions to drugs may be *mild*, with symptoms such as ______________________________

____

20. Allergic reactions to drugs are more common in patients with ________________________________

____

21. *Severe* allergic reaction with shock, laryngeal edema, and dyspnea is called ____________________

____

22. Treatment of severe anaphylactic reactions can include the following: ________, _________, and

____

23. What is the fastest-acting route of administration?

a. oral

b. rectal

c. transdermal

d. intravenous

24. What is the most common and easiest route of administration?

a. IV

b. IM

c. PO

d. PR

25. Which route is used when only a local effect is desired?

a. topical

b. transdermal

c. oral

d. otic

Chapter 4

Medication Preparations and Supplies

Key Terms and Concepts

Caplet
Capsule
Drug form
Elixir
Emulsion
Enema
Enteric-coated tablet
Inhalation drug forms
Injectable drug forms
Lozenge
Oral drug forms
Parenteral
Reconstitution
Rectal drug forms
Route of delivery
Solution
Suppository
Suspension
Sustained-release capsule or tablet
Syrup
Tablet
Topical drug forms

Objectives

Upon completion of this chapter, the learner should be able to:

1. Differentiate between various oral and rectal drug forms.
2. Describe the various injectable drug forms.
3. Define the following types of injections: intravenous (IV), intramuscular (IM), and intradermal (ID).
4. Explain how the different types of injections differ in administration and absorption.
5. Compare the IV injections referred to as IV push, IV infusion, and IV piggyback.
6. Contrast the various topical drug forms.
7. Explain the advantages of administering drugs via a transdermal patch.
8. Describe inhalable drug forms.
9. Identify various supplies used in the preparation of medications.

The forms in which drugs are prepared are as numerous as the routes of administration. **Drug form** refers to the type of preparation in which the drug is supplied. Pharmaceutical companies prepare each drug in the form(s) most suitable for its intended **route of delivery** and means of absorption. *Drug form* and *drug preparation* are synonymous. There are many different dosage forms; in fact, the U.S. Food and Drug Administration lists over 140 different dosage forms. Table 4-1 lists abbreviations of some of the common drug forms and routes of administration.

Table 4-1 Common Abbreviations for Drug Administration

Drug Forms		Routes	
cap	capsule	Inh	inhaled
		ID	intradermal
		IM	intramuscular
elix	elixir	IV	intravenous
Gtt	Drop	TOP	topical
Inj	Injectable		
Patch	Patch		
Powder	Powder		
Soln	solution		
supp	suppository	PO, po	oral
susp	suspension	R or PR (per rectum)	rectal
Tab	tablet	SQ	Subcutaneous
T		TST	TB skin test

Drug Forms and Devices

You probably have received medications in many of the standard forms at some time during your life. Each form is defined and listed in the following sections according to the routes of administration. Figure 4-1 illustrates some examples of oral drug forms. Drugs may be administered through the gastrointestinal (GI) tract or parenterally. GI routes include oral, nasogastric or gastrostomy tube, and rectal. **Parenteral** technically refers to any route *not* involving the GI tract, including injection, topical (skin or mucosal), transdermal, and the inhalation route. The parenteral route has become known as the "injectable" route and the topical, transdermal, and inhalation routes are routes that stand in a category often labeled "other routes."

Oral Drug Forms

Oral drug forms include the following and are summarized in Figure 4-1 with visuals to help you distinguish between the forms:

Tablet. Tablets (Figure 4-1A) are disks of compressed drug. They may be a variety of shapes and colors, may be coated to enhance easy swallowing, and may be *scored* (evenly divided in halves or quarters by score lines) to enhance equal distribution of the drug if the tablet has been broken (Figure 4-1B). One specific type of table is a **caplet**, an oblong form of a tablet (Figure 4-1C).

Enteric-coated tablet. This is a tablet with a special coating that resists disintegration by gastric juices (Figure 4-1D). The coating dissolves further down the

GI tract in the enteric, or intestinal, region. Some drugs that are irritating to the stomach, such as aspirin, are available in enteric-coated tablets. To be effective, the coating must never be destroyed by chewing or crushing when the tablet is administered. This is why patient education and auxiliary labels are very important to ensure that patients do not crush or split certain medications.

Capsule. The drug is contained within a gelatin-type container (Figure 4-1E).

- Easier to swallow than noncoated tablets.
- Double chamber may be pulled apart to add drug powder to soft foods or beverages for patients who have difficulty swallowing (unless specifically contraindicated for absorption).

Sustained-release capsule or tablet. Capsule or tablet (Figure 4-1D, E) containing drug particles that have various coatings (often of different colors) that differ in the amount of time required before the coatings dissolve. This form of drug preparation is designed to deliver a dose of drug over an extended period of time. An advantage of taking a drug in the sustained-release form is the decreased frequency of administration. For example, the antihypertensive Cardizem may be administered in tablet form 60 mg tid (three times daily) or in the sustained-release form (Tiazac 180 mg) only once daily. Because of the significance of the various coatings that encapsulate the drug particles, it is important that the small colored pellets or any sustained-release dosage form *not* be crushed or mixed with foods unless *specifically allowed* by the drug manufacturer. Damage to sustained-release dosage forms may result in the drug being released all at one time as it is administered. Such immediate release of the drug is a potential overdose. Sustained-release capsules or tablets should be swallowed whole, with no physical damage to the contents of the capsule.

Lozenge *(troche)*. Tablet containing palatable flavoring, indicated for a local (often soothing) effect on the throat or mouth (Figure 4-1H).

- Patient is advised *not* to swallow a lozenge; it should be allowed to slowly dissolve in the mouth.
- Patient is also advised *not* to drink liquids for approximately 15 minutes after administration, to prevent washing off of the lozenge contents from the throat or mouth.

Suspension. Liquid form of medication that must be shaken well before administration because the drug particles settle at the bottom of the bottle. The drug is not evenly dissolved in the liquid until the mixture is properly shaken (Figure 4-1I).

- A cephalosporin (cephalexin) suspension is a commonly used antibiotic suspension for children. This form is more easily ingested by children than are capsules of Keflex.
- Flavoring of suspensions is common, as many tend to have a bitter taste as a result of them being suspended in liquid, rather than dissolved.

Emulsion. Liquid drug preparation that contains oils and fats in water. These are typically topical or transdermal (Figure 4-1J).

Elixir or fluid extract. Liquid drug forms with alcohol base (Figure 4-1K).

- Should be tightly capped to prevent alcohol evaporation.
- Should not be available to alcoholics.
- Caution use in small children.

Syrup. Sweetened, flavored liquid drug form. Cherry syrup drug preparations are common for children (Figure 4-1L).

Solution. Liquid drug form in which the drug is totally and evenly dissolved. Appearance is clear rather than cloudy or settled (as with a suspension) (Figure 4-1M).

Many drug forms for the oral route are commonly available over the counter and include thousands of trade name products. The oral route is the easiest and probably the cheapest for administration. It is, however, *not* the route of choice for the treatment of emergencies, acute pain, nothing by mouth (NPO) patients (ordered to have nothing by mouth), or patients who are unable to swallow. Other routes, especially the parenteral routes, produce a more rapid absorption rate and drug effect due to the drug's often direct absorption into the bloodstream.

Rectal Drug Forms

Rectal drug forms include the following:

Suppository. Drug suspended in a substance, such as cocoa butter, that melts at body temperature.

Enema. Drug may be either a suspension (needs to be shaken before administration) or a solution to be administered as an enema.

The rectal route of administration is often the choice if the patient is ordered to be NPO or cannot swallow. The most common classifications of drugs given rectally include laxatives, sedatives, antiemetics (prevent vomiting), and antipyretics (reduce fever). A local analgesic effect may also be achieved by this route.

Injectable Drug Forms

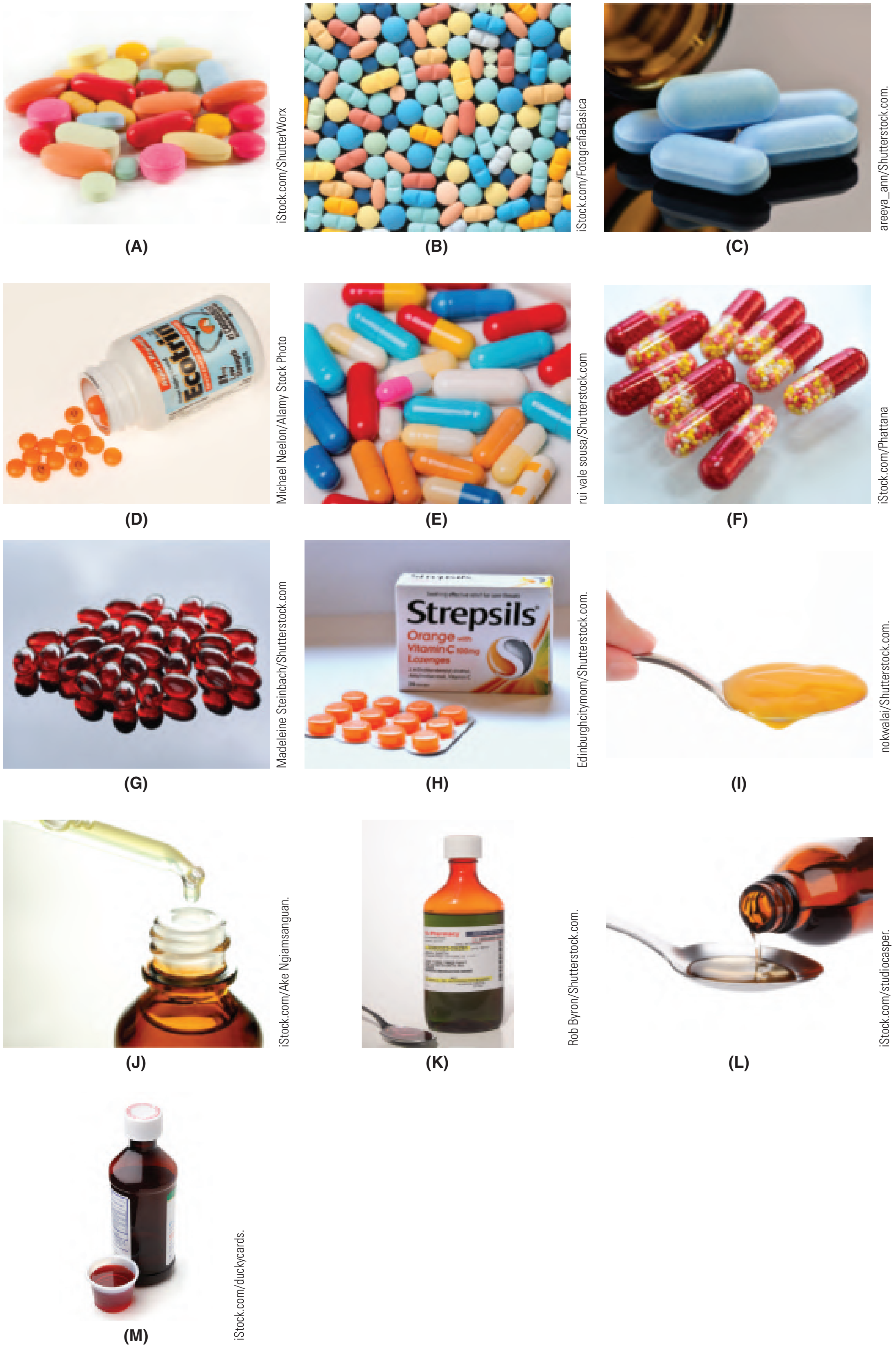
Injectable drug forms include the following:

Liquid. Drug suspended (suspension) or dissolved (solution) in a sterile vehicle.

- Quite often the solutions have a sterile water base and are thus referred to as aqueous (aq) (waterlike) solutions.
- Some solutions have an oil base, which tends to cause a more prolonged absorption time. The oily nature of these solutions makes them thick; thus, they are referred to as *viscous solutions*.

Powder. Dry particles of drugs. The powder itself cannot be injected. It must be mixed with a sterile diluting solution (sterile water or saline solution) to render an injectable solution. This is termed **reconstitution** of a drug. Drugs are supplied undiluted in powder form because of the short period of time they remain stable after dilution.

The various injection routes differ according to the type of tissues into which the drug is deposited and the rate of absorption.



(A) iStock.com/ShutterWorx

(B) iStock.com/FotografiaBasica

(C) areeya_ann/Shutterstock.com.

(D) Michael Neelon/Alamy Stock Photo

(E) rui vale sousa/Shutterstock.com

(F) iStock.com/Phattana

(G) Madeleine Steinbach/Shutterstock.com

(H) Edinburghcitymom/Shutterstock.com.

(I) nokwalai/Shutterstock.com.

(J) iStock.com/Ake Ngiamsanguan.

(K) Rob Byron/Shutterstock.com.

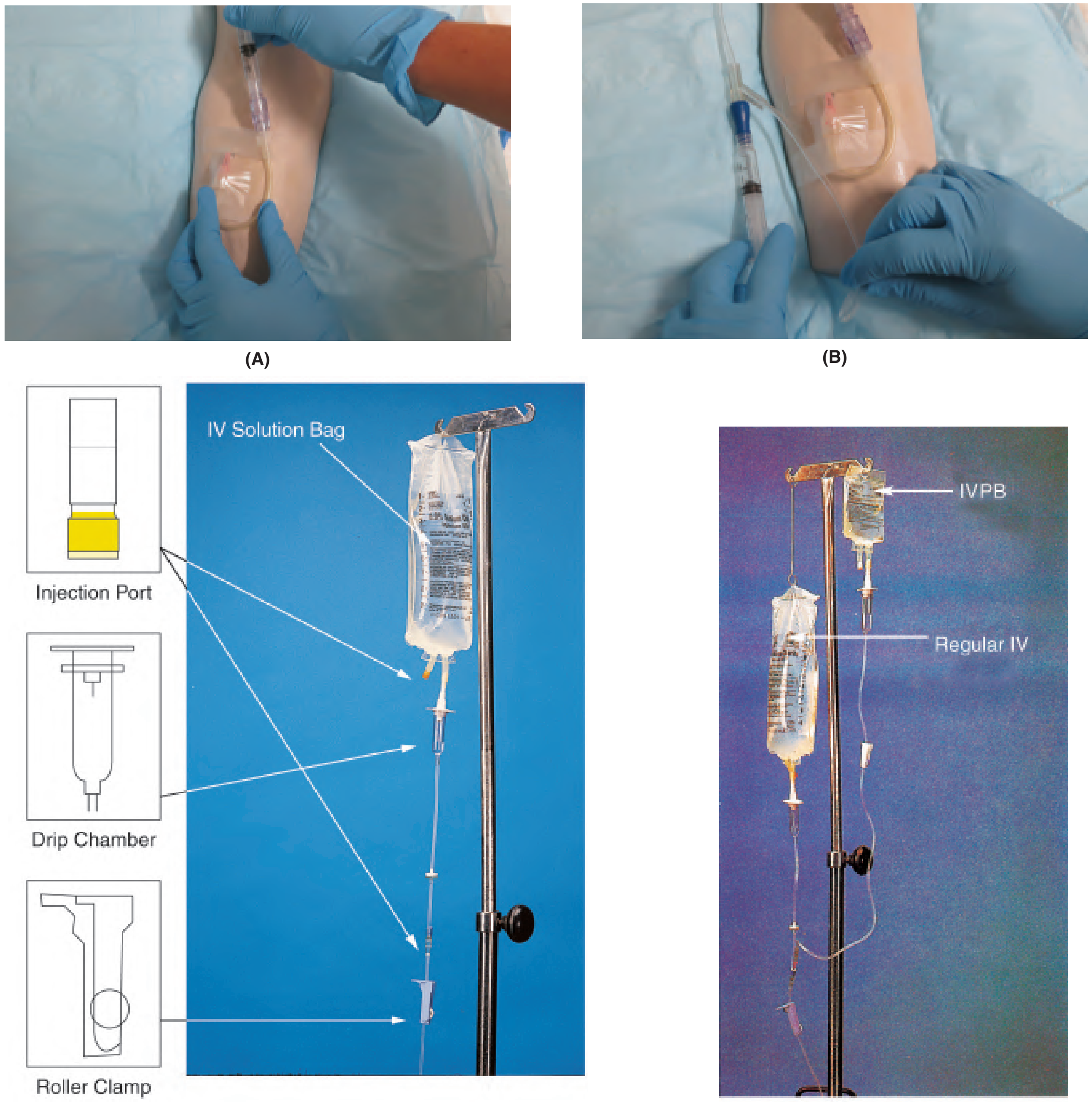
(L) iStock.com/studiocasper.

(M) iStock.com/duckycards.

Figure 4-1 Oral drug forms. Tablets and capsules vary in size, shape, and color. Liquid medications vary in viscosity and texture. (A) Tablet, (B) Scored tablet, (C) Caplet (D) Enteric-coated tablet, (E) Capsule, (F) Sustained-release capsule, (G) Gelatin capsule, (H) Lozenge (I) Suspension, (J) Emulsion, (K) Elixir, (L) Syrup, (M) Solution.

Intravenous. Injected directly into a vein. Immediate absorption and availability to major organs renders this route a dangerous one. IV drugs are usually administered by physicians, paramedics, or nurses. Types of IV injections include the following:

- IV push—a small volume of drug (bolus) injected into a peripheral saline lock (PRN adapter), attached to a vein (Figure 4-2A). An IV push medication can also be injected into a port on a primary (continuous) injection line (Figure 4-2B).



(A) (B)

(C) (D)

Figure 4-2 Intravenous (IV) administration. Different forms of IV injection include (A) IV push, injecting a bolus of medication into a peripheral saline lock; (B) pinch closed the IV tubing of a primary infusion line to administer an IV push medication; (C) IV infusion (continuous); and (D) IV piggyback (IVPB) intermittent.

Note

When adding a medication to an IV solution bag through the injection port, take the bag down and invert it a few times so the drug will be dispersed throughout the solution instead of remaining concentrated at the bottom of the bag.

- IV infusion or IV drip—a large volume of fluids, often with drugs added, that infuses continually into a vein (Figure 4-2C).
- IV piggyback (IVPB)—a drug diluted in moderate volume (50–100 mL) of fluid for intermittent infusion at specified intervals, usually q6–8h; the diluted solution is infused (piggyback) into a port on the main IV tubing or into a rubber adapter on the IV catheter (Figure 4-2D).

Intramuscular. Injected into a muscle by positioning the needle and syringe at a 45- to 90-degree angle from the skin (Figure 4-3). Absorption is fairly rapid due to the vascularity (presence of many blood vessels) in muscle. In most cases, a 1-inch needle is used for IM injections, but for a smaller person or a child, a ⅝-inch needle is sometimes more appropriate.

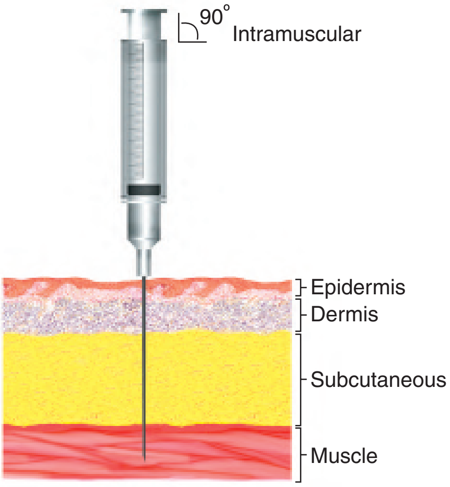


Figure 4-3 Intramuscular (IM) injection. Needle is inserted at a 90-degree angle.

Subcutaneous. Injected into the fatty layer of tissue below the skin by positioning the needle and syringe at a 45-degree angle from the skin (Figure 4-4). Commonly, a ⅝-inch needle is used for subcutaneous injections. This may be the route of choice for drugs that should not be absorbed as rapidly as through the IV or IM routes. Sometimes, especially with self-administration or a shorter needle, a 90-degree angle is used.

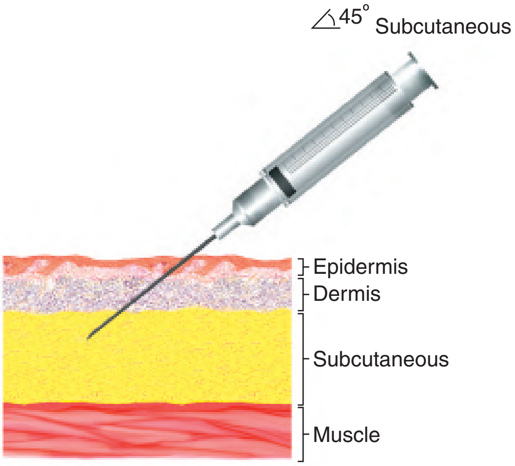


Figure 4-4 Subcutaneous injection. Needle is usually inserted at a 45-degree angle. Sometimes, with a shorter needle (3/8-inch), a 90-degree angle is used.

Intradermal. Injected just beneath the skin by positioning the needle bevel up and the syringe at a 15-degree angle from the skin (Figure 4-5). This route is used primarily for allergy skin testing. Because of the lack of vascularity in the dermis, absorption is slow. The greatest reaction is in the local tissues rather than systemic. When a small amount (0.1–0.2 mL) of drug is injected intradermally, the amount of redness that develops around the injection site can be used to determine whether a person is sensitive to the drug. Tuberculin (TB) skin tests (TST) are also administered intradermally, and the site is inspected 48–72 h later for hardness (induration) and swelling. Redness (erythema) alone, *without swelling*, does not indicate a positive test result with PPD. The *raised area* (*induration*) is measured with a special ruler and the number of millimeters (mm) is documented. Check with your local public health department regarding appropriate protocol with a positive TST test result. A TB syringe is also used for allergy testing, where a minute amount of an allergen is injected into the ID area.

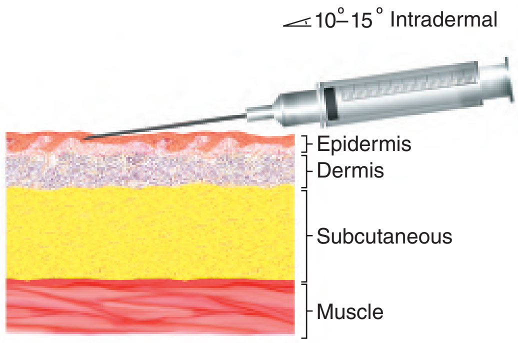


Figure 4-5 Intradermal injection. Needle is inserted just beneath the skin at a 10- to 15-degree angle. Bevel of needle is up.

Epidural. While not typically utilized in the outpatient setting, it is still important to have knowledge of epidural injections. This administration is typically done by a physician. This route injects medication into a catheter that has been placed by an anesthesiologist in the epidural space of the spinal canal. Medications for pain can be administered into the catheter by bolus (a measured amount of solution in a syringe) or by continuous infusion through tubing attached to a bag of solution. Epidural catheters have long been used for the administration of opioid analgesics for chronic intractable pain and for chemotherapy. Epidurals have become a popular and widely accepted vehicle for the management of acute postoperative pain.

The less common parenteral routes, which are usually limited to a physician's administration, with some exceptions, are as follows:

Intraosseous. Injected directly into the marrow of long bones. This route may be used to administer medications during a cardiac arrest or other emergency situations when traditional IV access is not available. (The intracardiac route is no longer recommended in Advanced Cardiac Life Support guidelines.)

Intraventricular. Drugs injected directly into the brain via a catheter (called a ventriculostomy) placed in a brain ventricle. In critical care, antibiotics can be given via a ventriculostomy tube.

Intraspinal. Injected into the subarachnoid space, which contains cerebrospinal fluid that surrounds the spinal cord. Drugs injected by this route are frequently anesthetics, which render a lack of sensation to those regions of the body distal to the intraspinal injection.

Intracapsular (intra-articular). Injected into the capsule of a joint, usually to reduce inflammation, as in bursitis. Arthritic or bursitic joints often injected with anti-inflammatory drugs include shoulders, elbows, wrists, ankles, knees, and hips.

Topical Form

Topical drug forms include drugs for dermal application and drugs for mucosal application. Those for dermal application include the following:

Cream or ointment. A semisolid preparation containing a drug, for external application. *Note*: Creams and ointments are not the same. The dose used differs for each. Also, creams tend to be more aqueous in nature, meaning they are composed of more water-based ingredients than an ointment is, which tends to be thicker or more viscous; this affects how they are used with different skin conditions.

Lotion. A liquid preparation applied externally for the treatment of skin disorders. Unlike hand lotions, medicated lotions (e.g., calamine lotion) should be *patted*, not rubbed, on the affected skin.

Liniment. Preparation for external use that is rubbed on the skin as a counterirritant. As such, the liniment creates a different sensation (e.g., tingling or burning) to mask pain in the skin or muscles.

Transdermal patch. Skin patch containing drug molecules that can be absorbed through the skin at varying rates to promote a consistent blood level of the drug between application times (Figure 4-6). Transdermal patches were first taken on the space shuttles during the 1990s for the prevention of nausea. Advantages of this method of administration include:

- Easy application, with minimal discomfort or undesirable taste
- Effectiveness for long periods of time—hours for some drugs, and days for others
- Consistent blood level of drug because the drug is released at varying rates rather than all at one time

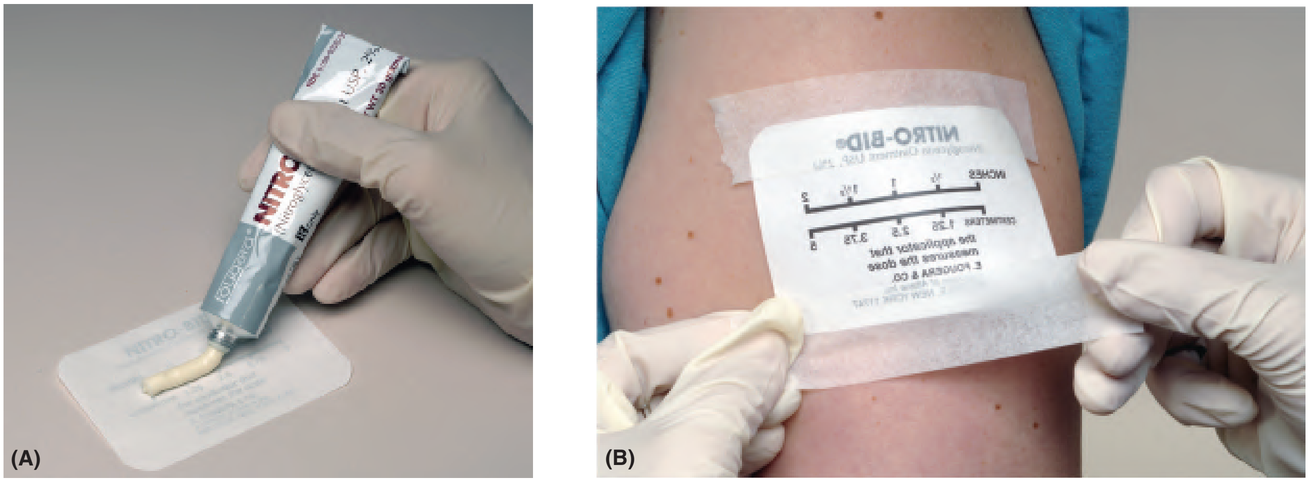


Figure 4-6 Topical administration. Dermal application includes creams and liquids placed on the skin. (A) Nitroglycerin ointment is measured on Appli-Ruler paper, and (B) paper containing ointment is applied to the skin and taped in place. Mark date and time on tape.

Transdermal patches vary in size, shape, and color. They are commonly seen today on patients for the prevention of angina. Current marketing of transdermal patches also includes others for the prevention of motion sickness (may be applied before traveling), management of chronic pain (e.g., Duragesic), use as a smoking deterrent (e.g., Nicoderm CQ), and estrogen replacement (e.g., Climara) or a birth control patch (e.g., Ortho Evra). Research is ongoing for the development of transdermal patches for high blood pressure, ulcers, allergies, and heart conditions. Probably not all drug molecules will be adaptable to this drug form, but this form certainly has opened new doors in the area of drug administration.

Both the transdermal patch and ointment are common forms for administration of nitroglycerin. Nitroglycerin is a vasodilator used for the treatment of angina (chest pain related to narrowing of the coronary arteries). The advantage of the external applications of nitroglycerin is their ability to *prevent* angina by the slow, consistent release of the drug over a period of time. Before the external applications became available, nitroglycerin was primarily available in the form of a sublingual tablet to be taken at the time of an angina attack. Now all three forms are used—the tablet, the ointment, and the patch—with the external forms focusing on the prevention of angina. They are applied at regular intervals, as follows:

Ointment. One to two inches measured and applied q8h (every eight hours) on special Appli-Ruler paper (Figure 4-6).

Transdermal patch. One patch (available in varied doses) usually applied for 12–14 h per day and then removed. Other types of patches are applied every 24–72 h depending on the condition treated (Figure 4-7).

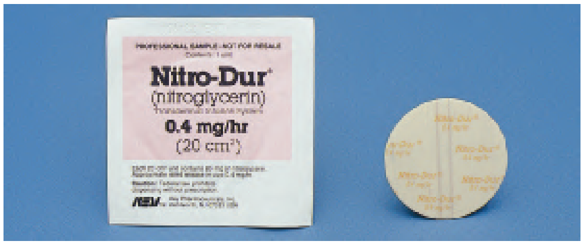


Figure 4-7 Nitro-Dur is a transdermal system of delivering medication used for prevention and long-term management of angina pectoris.

Other drug preparations considered topical are those that are applied to *mucosal membranes*. Some are administered for local effect (at the site of application), and in other cases, a systemic (affecting the whole body) effect is desired. The *mucosal drug forms* include the following:

Eye, ear, and nose drops (gtt). Drugs in sterile liquids to be applied by drops (referred to as instillation of drops).

Eye ointment. Sterile semisolid preparation, often antibiotic in nature, only for ophthalmic use.

Vaginal creams. Medicated creams, often of antibiotic or antifungal nature, to be inserted vaginally with the use of a special applicator.

Rectal and vaginal suppositories. Drugs suspended in a substance, such as cocoa butter, that melts at body temperature, for local effect. Some rectal suppositories are also used for systemic effects, for example, Tylenol suppository for fever (Figure 4-8).

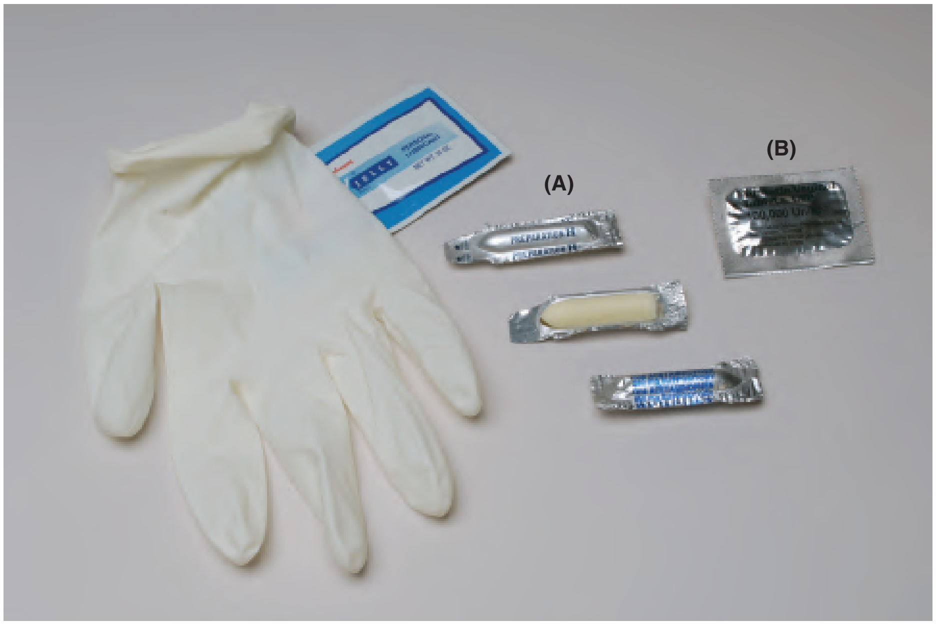


Figure 4-8 Topical administration via mucous membranes. Suppositories are available in various shapes and sizes, for example, (A) rectal suppositories, wrapped in foil and unwrapped, and (B) vaginal suppository, wrapped in foil. Lubricant and a glove will be needed for administration.

Douche solution. Sterile solution, often an antiseptic such as povidone–iodine solution and sterile water, used to irrigate the vaginal canal.

Buccal tablet. Tablet that is absorbed *via the buccal mucosa* in the mouth.

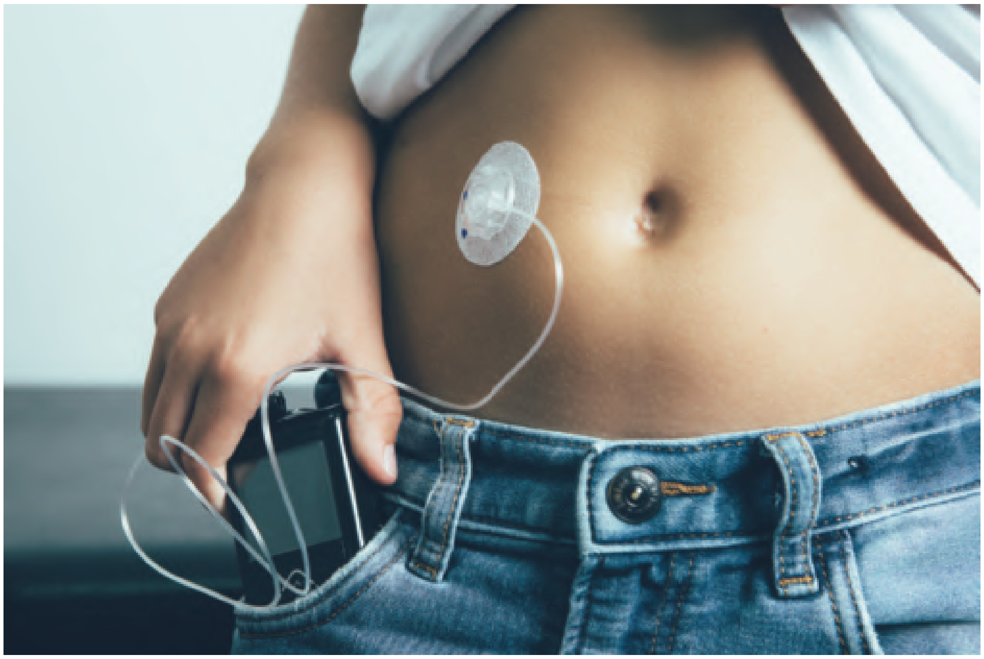
- Patient should be told *not* to swallow the tablet; it is to be placed between the cheek and gums and allowed to dissolve slowly.
- Not commonly used today. A sublingual tablet is preferable.

Sublingual tablet. Tablet that is absorbed via the mucosa under the tongue.

- Patient should be told *not* to swallow the tablet; it is to be placed under the tongue and allowed to dissolve slowly.
- The most common sublingual tablet is nitroglycerin. Given for the treatment of angina, this drug reaches the bloodstream immediately via the rich vascular supply of sublingual capillaries. Angina may be relieved within one to five minutes after sublingual nitroglycerin is administered.

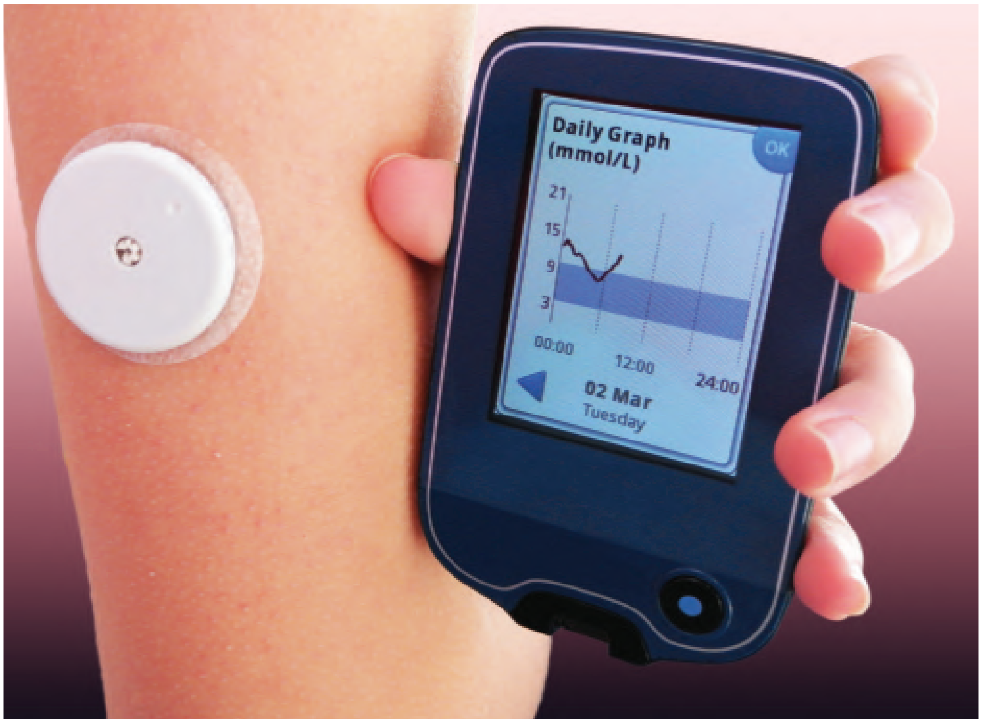
Implantable Devices

Implantable devices are available in a variety of sizes and are placed just below the skin near blood vessels, where the medication can readily be absorbed into the bloodstream. One example is a small infusion pump called an insulin pump, which is implanted in the subcutaneous tissue of a patient with diabetes and programmed to deliver a continuous supply of insulin (Figure 4-9). Many pumps integrate with a continuous glucose monitor (CGM) (Figure 4-10) through applications on smartphones, allowing the insulin delivery to be adjusted. There are two main types of insulin pumps: tubed and tubeless. Tubed insulin pumps have two parts—a cannula, which is attached to the skin at one end and the pump at the other, and the pump, which contains the insulin reservoir. The cannula is replaced every few days. The cannula can be disconnected from the



Click and Photo/Shutterstock.com.

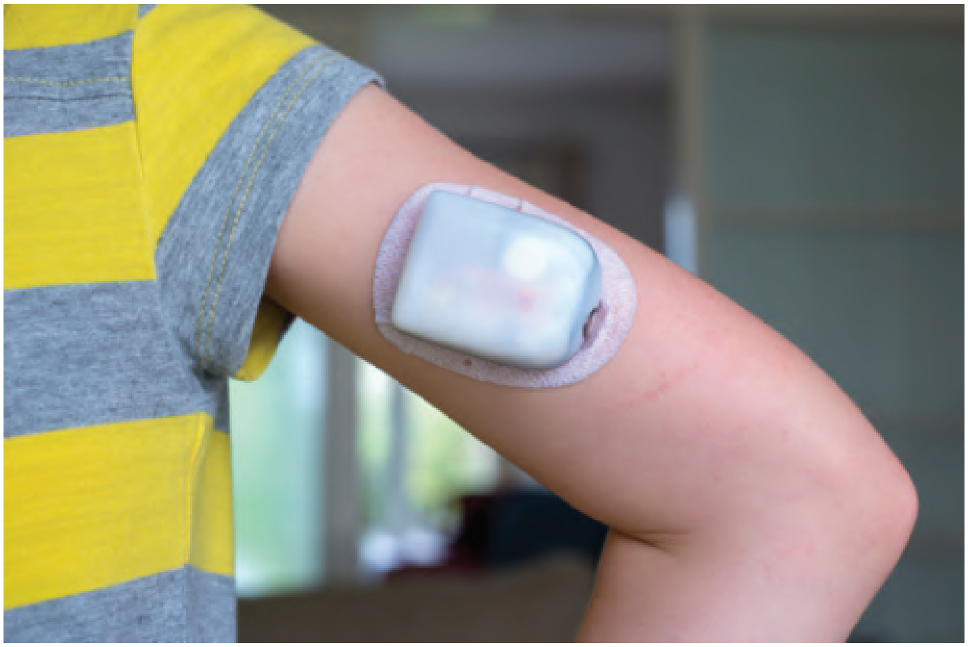
Figure 4-9 An insulin pump is a wearable device that delivers insulin continuously.



Dragoljub Bankovic/Shutterstock.com

Figure 4-10 An example of a continuous glucose monitor (CGM).

pump for activities such as showering or swimming. Tubeless pumps (often called patch pumps) have a cannula under the skin, but the insulin reservoir and cannula are part of a pod that sits on the skin (Figure 4-11). Each patch or pod is used one time and is changed every two to three days (or sooner if it runs out of insulin). Tubeless pumps are waterproof and remain in place for showering or swimming. Implantable devices are also used to deliver contraceptives and to administer chemotherapeutic drugs to cancer patients.



loocmill/Shutterstock.com

Figure 4-11 A tubeless (patch) insulin pump.

Another recent and innovative drug form entails sandwiching the drug between very thin plastic membranes and then placing it under the patient's eyelid. This administration permits a controlled release of medicine over an extended time period. Pilocarpine, which is used to treat glaucoma, has been successfully administered in this manner with little or no discomfort.

Inhalation Drug Forms

The inhalation route is a very fast-acting (second to IV route) and effective route for delivering humidification and medication directly into the respiratory system. Usually, a liquid drug is placed in a device that will create a fine mist or aerosol that contains tiny droplets of medication. The medication is rapidly absorbed into the respiratory system due to the large surface area and vast blood supply of pulmonary capillaries. The **inhalation drug forms** used for the inhalation route include:

Spray or mist. Liquid drug forms that may be inhaled as fine droplets via the use of spray bottles, nebulizers, or metered dose inhalers.

- In the hospital setting, respiratory therapists instill a liquid into a chamber of a nebulizer for a patient's breathing treatment. Often the liquid contains a bronchodilator, a mucolytic agent, or a sterile saline solution for moisture.
- In the home, the patient may instill aerosol sprays into the respiratory system via a small-volume nebulizer (SVN), a metered-dose inhaler (MDI), or a dry-powdered inhaler (DPI). These inhaler devices and how to use them will be explained in detail in the respiratory system chapter. Patients with moderate-to-severe asthma rely on these devices to keep their airways open by inhaling the mist of a bronchodilator to open constricted airways and the mist of an anti-inflammatory agent to reduce swollen airways. Patients with mild asthma use their inhalers when needed (PRN) to treat or prevent mild episodes.

Supplies

Note

In some areas, a physician's order is required for pill crushing. Check the regulations in your area. The homepage of the Institute for Safe Medication Practices website contains an up-to-date "Do Not Crush" list under the heading "Medication Safety Tools & Resources."

Considering the variety of drug forms you may be administering, you must become familiar with various supplies to be used:

Medicine cup. Two types of disposable cups are commonly used. Paper cups are used for dispensing tablets and capsules. Plastic 1-oz medicine cups with measurements (mL, tsp, tbsp, or oz) marked on the side are used for dispensing oral liquid medications.

Individual pill crusher and pill cutter. Used in most institutions (Figure 4-12). Various other pill-crushing devices are available.

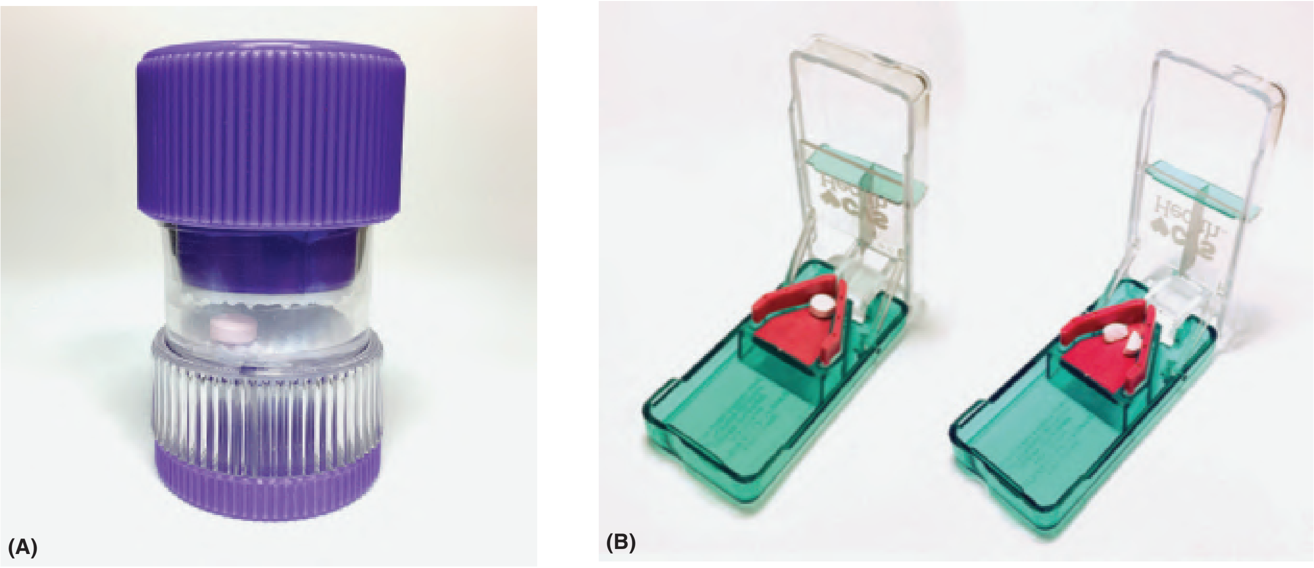


Figure 4-12 (A) A plastic pill crusher. (B) A plastic pill splitter to break scored tablets, if necessary.

Medication for injection is contained in an ampule, a vial, or a prefilled syringe (Figure 4-13) or a pen (Figure 4-14):

Ampule. Small glass container that holds a single dose of sterile solution for injection. The ampule must be broken at the neck to obtain the solution. Ampules pose the risk of cuts to the user or glass getting into the medication. There are reuseable or disposable ampule breakers that increase safety when using an ampule. Additionally, filter needles are used to draw up the medication out of the ampule to protect against injecting shards of glass.

Vial. Glass container sealed at the top by a rubber stopper to enhance the sterility of the contents. Contents may be a solution or a powdered drug that needs to be reconstituted. Vials may be multiple dose or unit dose.

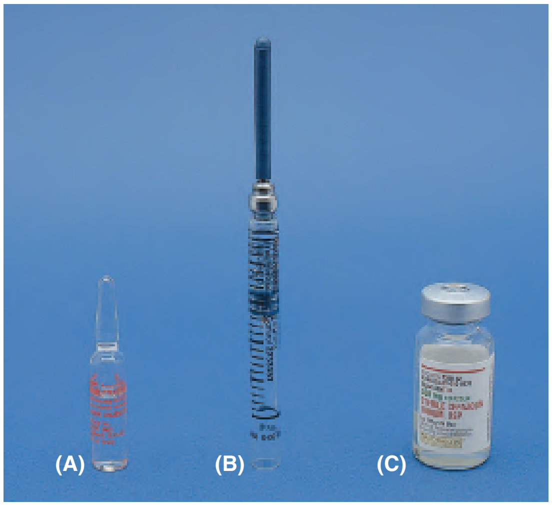


Figure 4-13 Medications given parenterally. (A) Ampule, (B) sterile cartridge with premeasured medication, and (C) vial of powder for reconstitution.

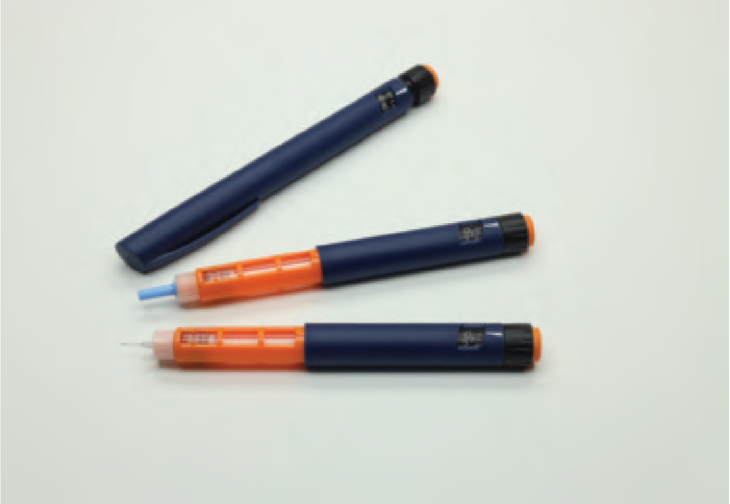

richir/Shutterstock.com.

Figure 4-14 Injector pens. Very commonly used for insulin administration.

- Multiple-dose vials contain large quantities of solution (up to 50 mL) and may be entered repeatedly through the rubber stopper to remove a portion of the contents. They contain a preservative that prevents microbial growth.
- Unit-dose vials contain small quantities of solution (1–2 mL) that are removed during a single use. Unit-dose vials are widely used today as a means of controlling abuse or removal of excess amounts of solution from a drug vial.

Needles. Needles for injections have two measurements—length and gauge—that must be noted (Figure 4-15).

- Length varies from short (⅜ inch) to medium (1–1½ inch) for standard injections. Long needles (5 inches) may be used for intraspinal or intraosseous routes. Needles that are 2–5 inches long are used for intra-articular injections (into the joint).

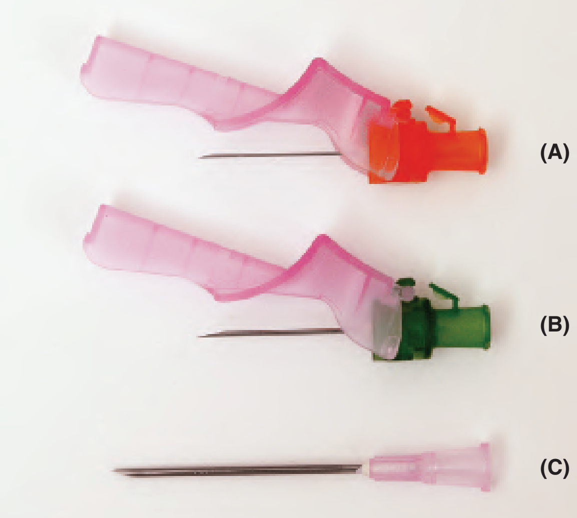


Figure 4-15 Examples of some various gauges and lengths of needles. (A) 25-gauge, 1-inch needle with safety cap; (B) 21-gauge, 1-inch needle with safety cap; and (C) 18-gauge, 1½-inch needle.

- Gauge is a number that represents the diameter of the needle lumen (opening). Needle gauges in common use by health care professionals vary from 16 (largest) to 31 (smallest), with the higher gauge number representing the smaller lumen. Occasionally, larger needles may be used; for example, physicians sometimes use a larger needle gauge for certain biopsies.

Syringes. Figure 4-16A shows the various parts of a typical syringe. The three most common disposable syringes used for parenteral administration of drugs are the standard hypodermic syringe, the tuberculin (TB) syringe, and the insulin syringe (Figure 4-16B).

- The standard hypodermic syringe has a capacity of 2–3 mL. Most companies prepackage this type of syringe with a needle attached. You may use this type of syringe for either subcutaneous or IM injections, so you must choose the package with the needle length and gauge appropriate for the route and depth of injection you will give. All hypodermic syringes are marked with 10 calibrations per milliliter (mL). Thus, each small line represents 0.1 mL. When preparing for an injection with this syringe, you must know the amount of solution needed to the nearest 0.1 mL.
- The insulin syringe is used strictly for administering insulin to diabetics. Insulin should be measured only in an insulin syringe. The standard insulin syringe has only a 1-mL capacity, which is equivalent to 100 units of U-100 insulin. The standard U-100 syringe has a dual scale: even numbers on one side and odd numbers on the other side. Look carefully at the calibrations on each side. Count each calibration (on one side only) as two units (refer to Figure 4-16A).

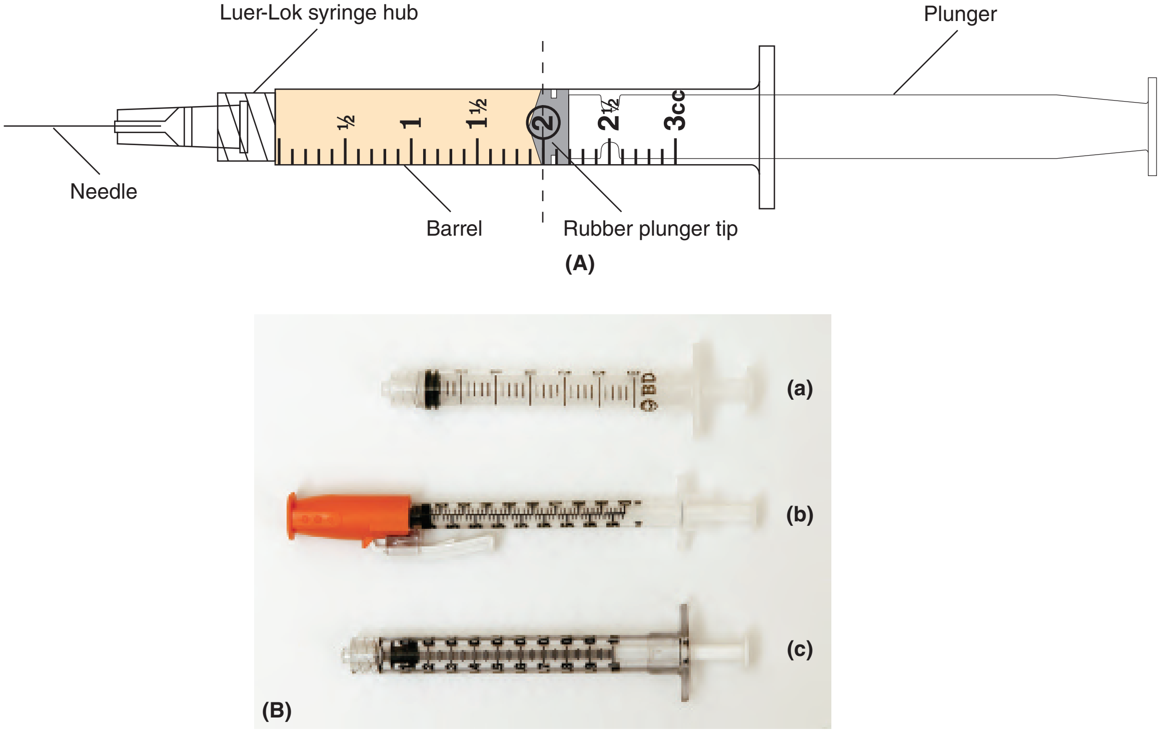


Figure 4-16 (A) Parts of a syringe. (B) Types of syringes: (a) 3-mL syringe, (b) standard U-100 insulin, and (c) 1-mL tuberculin with Luer-Lok.

- The TB syringe is very narrow and is finely calibrated. Like the insulin syringe, the total capacity is only 1 mL. There are 100 fine calibration lines marking the capacity. Thus, each line represents 0.01 mL. Every tenth line is longer, to indicate 0.1-mL increments. Very precise small amounts of solution may be measured with the TB syringe. It is most commonly used for newborn and pediatric dosages and for ID skin tests. When preparing for an injection with this syringe, you must know the amount of solution needed to the nearest 0.01 mL.

There are also smaller insulin syringes to more accurately measure small amounts of insulin, such as those for children. Look carefully at the calibrations. In these Lo-Dose syringes, each calibration counts only *one* unit.

It is extremely important that you interpret the value of the calibrations on each of the syringes. Study the calibrations each time you prepare for an injection to prevent a medication error from occurring due to negligent misinterpretation. *All insulin dosages must be double-checked by two caregivers before administration.*

Oral syringes. Health care professionals should be aware that some oral liquid medications are dispensed from the pharmacy in disposable plastic syringes with rubber or plastic covers on the tip. These syringes are labeled “Not for injection” or “For oral use only.”

Safety Devices

The Occupational Safety and Health Administration (OSHA) has mandated that every effort be made to reduce the risk of needle-stick injuries that could lead to exposure to blood-borne pathogens, such as the human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV). Therefore, the following equipment is included in OSHA recommendations:

- Safety needles with a protective sheath that covers the needle automatically immediately after administration, or others that retract into the syringe upon administration
- Needleless devices that can be used to access IV tubing for the administration of IV push medications or IVPBs

Safety devices vary depending on the company manufacturing the equipment. Therefore, it is important that you familiarize yourself with the safety equipment used in your facility.

Chapter Review Quiz

Fill in the blanks

1. a. Which route of administration is used most often? Why?

____.

b. Which route is fastest? _______________________________

Complete with the appropriate drug form

2. A tablet placed under the tongue: _______________________

3. A tablet placed in the cheek pouch: _______________________

4. A tablet dissolved in the mouth for local action: _______________________

5. A coated tablet that dissolves in the intestines instead of in the stomach:

____

6. A tablet or capsule that has delayed action over a longer period of time:

____

7. A liquid drug form with an alcohol base: _______________________

8. A liquid medication that must be shaken before administration:

____

9. Drugs given by the rectal route include: _______________________

____

10. The parenteral route refers to any route other than the GI route. Name four parenteral routes:

____

____

____

Fill in the blanks

11. Topical drug forms include those applied to the _______________ and _______________.

12. Medicine for injection is contained in two types of glass containers:

a. With rubber stopper on top: _______________________

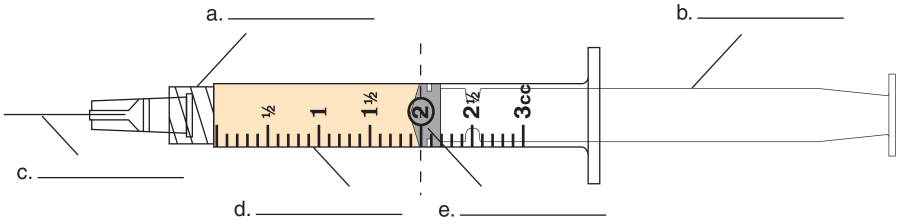
b. All glass to be broken at the neck: _______________________

13. Needles are selected according to two measurements: _______________ and _______________.

14. The three most commonly used syringes for injections are _______________, _______________, and _______________.

Labeling

15. Label the parts of a syringe.



Multiple choice

16. Which of the following are inhalation drug forms? (Select all that apply.)

a. mist

b. spray

c. dry powder inhaler

d. emulsion

e. suspension

17. Which of the following is an advantage of the transdermal patch?

a. easy application

b. inconsistent absorption

c. effective for short periods of time

d. no systemic effects

18. Which statement is correct?

a. IV drips are a way of administering large volumes of fluids.

b. IV push is a way of administering large volumes of fluids.

c. IVPB is a way of administering large volumes of fluids.

d. There is no way to administer large volumes of fluids via the IV route.

19. Which of the following routes has the slowest absorption?

a. intradermal

b. intramuscular

c. subcutaneous

d. intravenous

20. Which angle is most commonly used to administer an intramuscular injection in adults?

a. 90 degrees

b. 45 degrees

c. 15 degrees

d. 10 degrees

Chapter 5

Abbreviations and Systems of Measurement

Key Terms and Concepts

Base
Computerized physician order entry (CPOE)
Conversion of units
Electronic medication administration record (eMAR)
e-prescribing (eRx)
Exponent
Factor-label method
Household system
Medical abbreviations
Medication orders
Metric system
Telephone order (TO)

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify common abbreviations and symbols used for medication orders.
2. List the six parts of a medication order and the two additional items required as part of a prescription.
3. Describe the responsibilities of a health care professional regarding verbal and telephone orders for medications.
4. Interpret medication orders correctly.
5. Define the three systems of measurement.
6. Convert dosages between and within systems of measurement.
7. Describe appropriate patient education for those who will be measuring and administering their own medications.

Abbreviations

Interpretation of the medication order is the first responsibility of a health care professional when preparing medication for administration. Interpreting medication orders is a form of written communication that is of critical importance for health care providers. Knowledge of **medical abbreviations** and symbols is essential for accurate interpretation of the physician's order. You must be familiar with the common abbreviations and symbols in Table 5-1. Orders may vary in the use of capital versus lowercase letters. You may occasionally come across other abbreviations not included in this list. *When in doubt, always question the meaning. Never guess!*

Table 5-1 Common Abbreviations for Medication Orders

Abbreviation	Meaning	Abbreviation	Meaning
a	before	mEq	milliequivalent
ac	before meals	mg	milligram
AD	Right ear	ml, mL	milliliter (equivalent to cc)
AM, am	Morning	mm	millimeter
AS	left ear	NEB	nebulizer
AU	both ears	NG	nasogastric
bid	twice a day	NPO, npo	nothing by mouth
cap	Capsule	NS, N/S, NSS	normal saline (sodium chloride, 0.9%)
cm	centimeter	OD	right eye
c̄	with	ODT	orally disintegrating tablet
D/C, dc	Discontinue	OS	Left eye
D5W	dextrose 5% in water	OU	both eyes
DS	double strength	oz	Ounce
EC	enteric coated	p	After
ER	extended release	pc	after meals
g, gm	Gram	PM, pm	afternoon
gr	grains	po, PO	by mouth, orally
gtt	Drop	PRN, prn	whenever necessary or as needed
h, hr	Hour	q2h	every 2 hours
Hs	bedtime	qh	every hour
IM	intramuscular	qid	four times a day
IV	intravenous	qs	quantity sufficient
IVPB	intravenous piggyback	R, pr	rectal, per rectum
kg, Kilo	kilogram	RL, R/L	Ringer's lactate
KVO	keep vein open	s̄	without
LA	long acting	SQ[a]	subcutaneous
L	liter	SL	sublingual
LR	Lactated Ringer's	SR	sustained release
mcg	microgram	stat	immediately and once only
supp	suppository	TO	telephone order

Abbreviation	Meaning	Abbreviation	Meaning
tab	tablet	tsp, t	teaspoon
tbsp, T, tbs	tablespoon	Vag/PV	vaginal
tid	three times daily	VO	verbal order

Note: Abbreviations should be written without periods. Also, some abbreviations in this table are on the ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations, but it is still important to know them

[a] *Subcutaneous* (SQ) is an example of an abbreviation noted on the ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations. When handwritten, they can be confused for other terms. Therefore, you may also notice "subcu" or "subcutaneous" written out in your clinical setting. With the expected near-future universal implementation of electronic records and electronic charting, handwritten look-alike errors will hopefully become a thing of the past. In fact, most facilities have already implemented electronic systems, so the majority of medical orders and prescriptions are no longer handwritten.

The *Institute for Safe Medication Practices* (*ISMP*) monitors and categorizes medication errors. Its purpose is to identify practices that have contributed to medication errors. The ISMP has published a list of problematic abbreviations, *ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations* (Figure 5-1). In addition, the Joint Commission has provided a minimum list of "official do not use" abbreviations that have been prohibited since June 2019. Items required to be on an organization's "Do Not Use" list are highlighted with a double asterisk (**) in the ISMP list (Figure 5-1).

Another safety practice requires the avoidance of periods in all medical abbreviations. If poorly written, the period could be mistaken as the number 1 or a decimal, causing an error in dosage. In addition, before giving or taking any medication order, the patient's allergies should be reviewed.

Medication orders contain six parts:

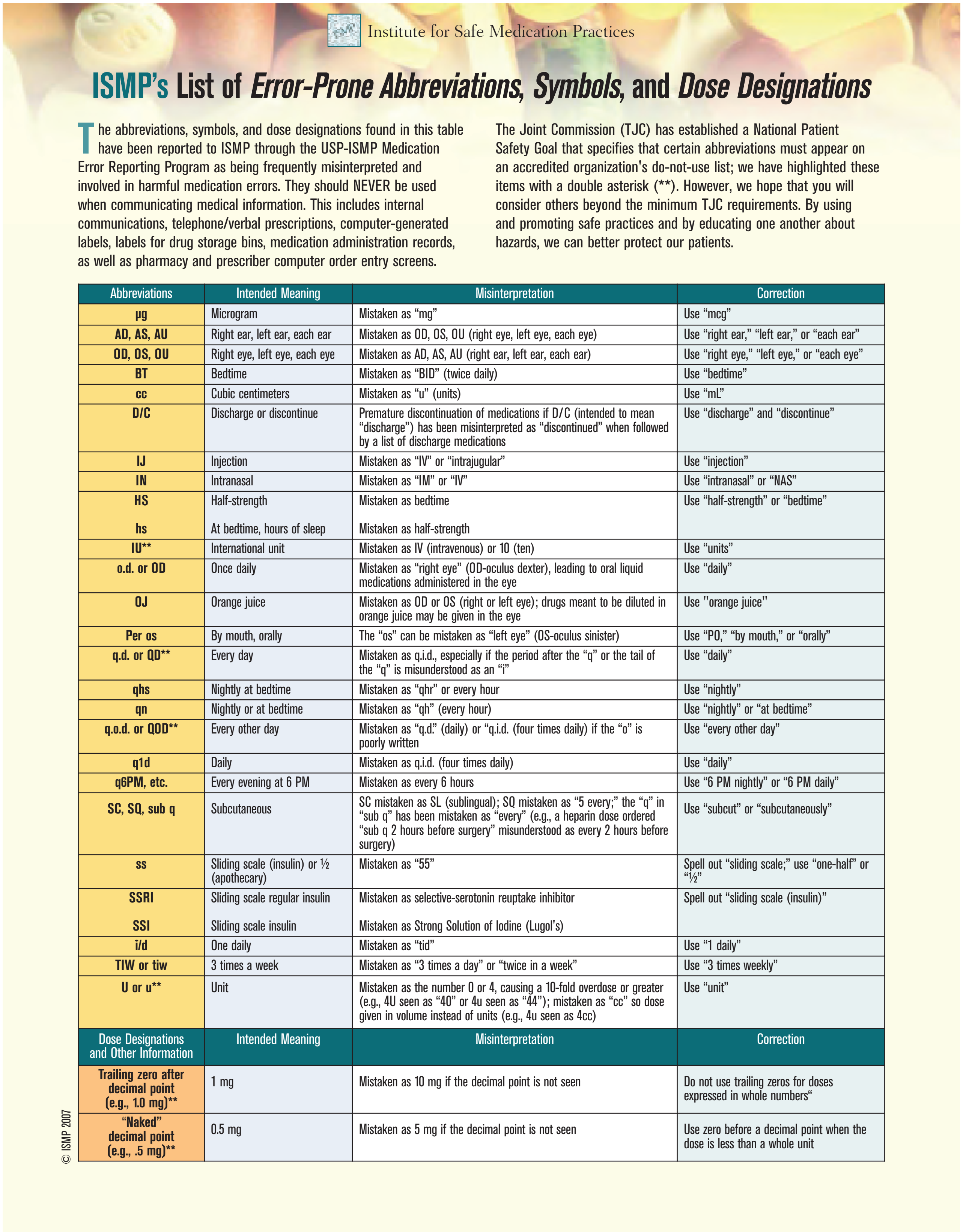
1. Date/time that the order was taken
2. Patient's name
3. Medication name
4. Dosage and/or amount of medication
5. Route or manner of administration (e.g., oral, subcutaneous)
6. Directions for use, including time to be administered and/or frequency

Medication orders must always be written and signed by a physician or other qualified health care professional. In certain circumstances, such as in an emergency or other situations per institutional policy, the physician may give a verbal order (VO). It is the responsibility of the health care professional to *read back and confirm the order* (i.e., medication and amount) before administration and to write down the medication, amount, and time of administration as soon as they are given. The physician will sign the medication order within a set time frame per policy.

Always determine the policy of the agency before taking a **telephone order (TO)**. Some agencies require a registered nurse to take TOs. In other facilities, licensed practical (vocational) nurses are allowed to take TOs. When taking a TO, always obtain the name of the person calling in the order and write next to the medication ordered the name of that person and the time the call was made, for example, "TO Dr. A. Smith, per Mary Jones, CMA at 1300." Also repeat all details regarding the medication, dosage, frequency, and so on as you write down the order.

Note

Regulations regarding phone orders vary from state to state. Check the rules in your state regarding who can call in an order and who can receive a phone order, as well as the time frame for the physician's signature.



Institute for Safe Medication Practices

ISMP's List of *Error-Prone Abbreviations, Symbols,* and *Dose Designations*

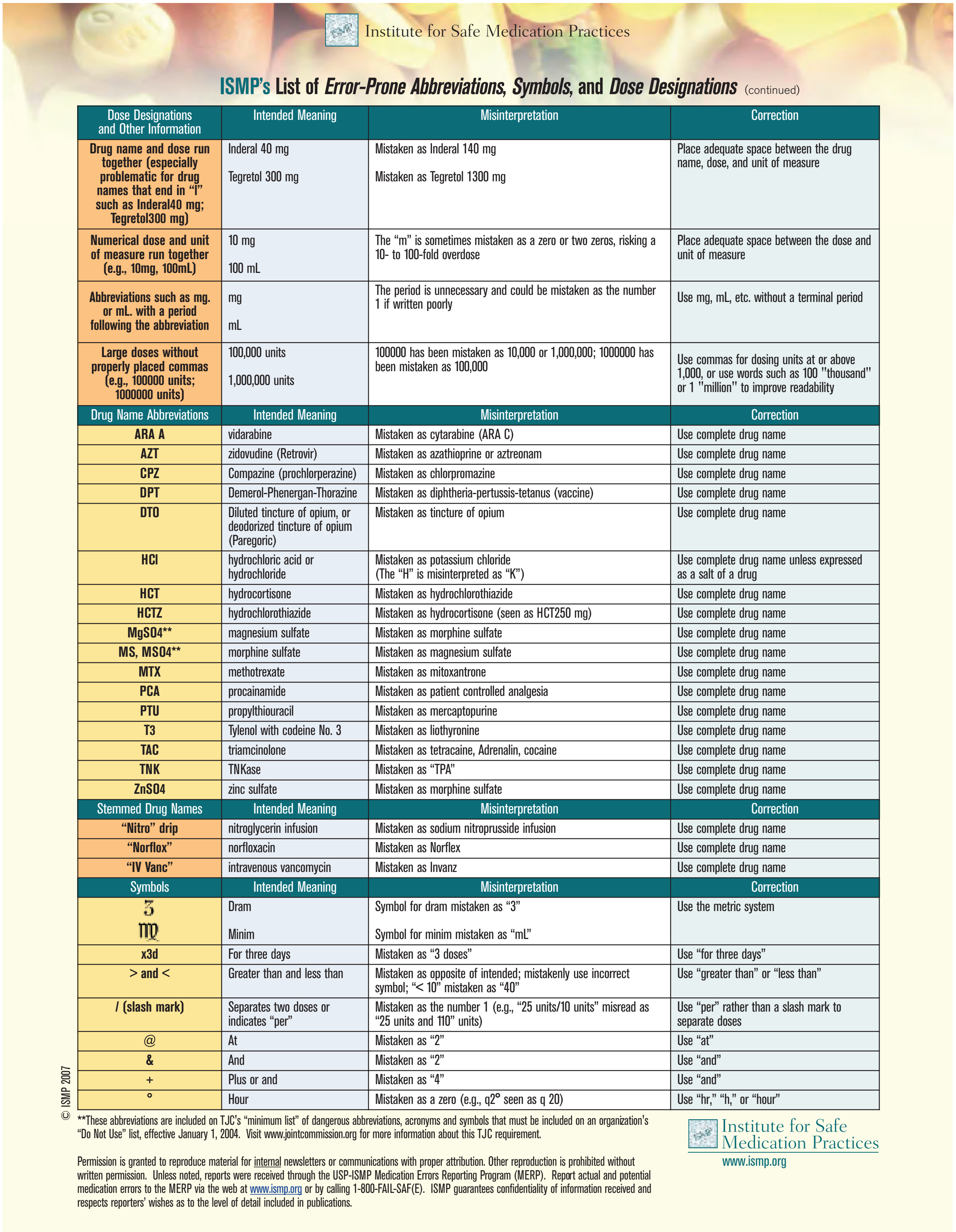
The abbreviations, symbols, and dose designations found in this table have been reported to ISMP through the USP-ISMP Medication Error Reporting Program as being frequently misinterpreted and involved in harmful medication errors. They should NEVER be used when communicating medical information. This includes internal communications, telephone/verbal prescriptions, computer-generated labels, labels for drug storage bins, medication administration records, as well as pharmacy and prescriber computer order entry screens.

The Joint Commission (TJC) has established a National Patient Safety Goal that specifies that certain abbreviations must appear on an accredited organization's do-not-use list; we have highlighted these items with a double asterisk (**). However, we hope that you will consider others beyond the minimum TJC requirements. By using and promoting safe practices and by educating one another about hazards, we can better protect our patients.

Abbreviations	Intended Meaning	Misinterpretation	Correction
µg	Microgram	Mistaken as "mg"	Use "mcg"
AD, AS, AU	Right ear, left ear, each ear	Mistaken as OD, OS, OU (right eye, left eye, each eye)	Use "right ear," "left ear," or "each ear"
OD, OS, OU	Right eye, left eye, each eye	Mistaken as AD, AS, AU (right ear, left ear, each ear)	Use "right eye," "left eye," or "each eye"
BT	Bedtime	Mistaken as "BID" (twice daily)	Use "bedtime"
cc	Cubic centimeters	Mistaken as "u" (units)	Use "mL"
D/C	Discharge or discontinue	Premature discontinuation of medications if D/C (intended to mean "discharge") has been misinterpreted as "discontinued" when followed by a list of discharge medications	Use "discharge" and "discontinue"
IJ	Injection	Mistaken as "IV" or "intrajugular"	Use "injection"
IN	Intranasal	Mistaken as "IM" or "IV"	Use "intranasal" or "NAS"
HS **hs**	Half-strength At bedtime, hours of sleep	Mistaken as bedtime Mistaken as half-strength	Use "half-strength" or "bedtime"
IU**	International unit	Mistaken as IV (intravenous) or 10 (ten)	Use "units"
o.d. or OD	Once daily	Mistaken as "right eye" (OD-oculus dexter), leading to oral liquid medications administered in the eye	Use "daily"
OJ	Orange juice	Mistaken as OD or OS (right or left eye); drugs meant to be diluted in orange juice may be given in the eye	Use "orange juice"
Per os	By mouth, orally	The "os" can be mistaken as "left eye" (OS-oculus sinister)	Use "PO," "by mouth," or "orally"
q.d. or QD**	Every day	Mistaken as q.i.d., especially if the period after the "q" or the tail of the "q" is misunderstood as an "i"	Use "daily"
qhs	Nightly at bedtime	Mistaken as "qhr" or every hour	Use "nightly"
qn	Nightly or at bedtime	Mistaken as "qh" (every hour)	Use "nightly" or "at bedtime"
q.o.d. or QOD**	Every other day	Mistaken as "q.d." (daily) or "q.i.d. (four times daily) if the "o" is poorly written	Use "every other day"
q1d	Daily	Mistaken as q.i.d. (four times daily)	Use "daily"
q6PM, etc.	Every evening at 6 PM	Mistaken as every 6 hours	Use "6 PM nightly" or "6 PM daily"
SC, SQ, sub q	Subcutaneous	SC mistaken as SL (sublingual); SQ mistaken as "5 every;" the "q" in "sub q" has been mistaken as "every" (e.g., a heparin dose ordered "sub q 2 hours before surgery" misunderstood as every 2 hours before surgery)	Use "subcut" or "subcutaneously"
ss	Sliding scale (insulin) or ½ (apothecary)	Mistaken as "55"	Spell out "sliding scale;" use "one-half" or "½"
SSRI **SSI**	Sliding scale regular insulin Sliding scale insulin	Mistaken as selective-serotonin reuptake inhibitor Mistaken as Strong Solution of Iodine (Lugol's)	Spell out "sliding scale (insulin)"
i/d	One daily	Mistaken as "tid"	Use "1 daily"
TIW or tiw	3 times a week	Mistaken as "3 times a day" or "twice in a week"	Use "3 times weekly"
U or u**	Unit	Mistaken as the number 0 or 4, causing a 10-fold overdose or greater (e.g., 4U seen as "40" or 4u seen as "44"); mistaken as "cc" so dose given in volume instead of units (e.g., 4u seen as 4cc)	Use "unit"
Dose Designations and Other Information	Intended Meaning	Misinterpretation	Correction
Trailing zero after decimal point (e.g., 1.0 mg)**	1 mg	Mistaken as 10 mg if the decimal point is not seen	Do not use trailing zeros for doses expressed in whole numbers“
"Naked" decimal point (e.g., .5 mg)**	0.5 mg	Mistaken as 5 mg if the decimal point is not seen	Use zero before a decimal point when the dose is less than a whole unit

© ISMP 2007

Figure 5-1 ISMP's list of error-prone abbreviations, symbols, and dose designations. Used with permission from the Institute for Safe Medication Practices, © ISMP 2015. Report actual and potential medication errors to the ISMP National Medication Errors Reporting Program (ISMP MERP) at 1-800-FAIL-SAF(E) or online at, www.ismp.org.



Institute for Safe Medication Practices

ISMP's List of *Error-Prone Abbreviations, Symbols,* and *Dose Designations* (continued)

Dose Designations and Other Information	Intended Meaning	Misinterpretation	Correction
Drug name and dose run together (especially problematic for drug names that end in "l" such as Inderal40 mg; Tegretol300 mg)	Inderal 40 mg Tegretol 300 mg	Mistaken as Inderal 140 mg Mistaken as Tegretol 1300 mg	Place adequate space between the drug name, dose, and unit of measure
Numerical dose and unit of measure run together (e.g., 10mg, 100mL)	10 mg 100 mL	The "m" is sometimes mistaken as a zero or two zeros, risking a 10- to 100-fold overdose	Place adequate space between the dose and unit of measure
Abbreviations such as mg. or mL. with a period following the abbreviation	mg mL	The period is unnecessary and could be mistaken as the number 1 if written poorly	Use mg, mL, etc. without a terminal period
Large doses without properly placed commas (e.g., 100000 units; 1000000 units)	100,000 units 1,000,000 units	100000 has been mistaken as 10,000 or 1,000,000; 1000000 has been mistaken as 100,000	Use commas for dosing units at or above 1,000, or use words such as 100 "thousand" or 1 "million" to improve readability

Drug Name Abbreviations	Intended Meaning	Misinterpretation	Correction
ARA A	vidarabine	Mistaken as cytarabine (ARA C)	Use complete drug name
AZT	zidovudine (Retrovir)	Mistaken as azathioprine or aztreonam	Use complete drug name
CPZ	Compazine (prochlorperazine)	Mistaken as chlorpromazine	Use complete drug name
DPT	Demerol-Phenergan-Thorazine	Mistaken as diphtheria-pertussis-tetanus (vaccine)	Use complete drug name
DTO	Diluted tincture of opium, or deodorized tincture of opium (Paregoric)	Mistaken as tincture of opium	Use complete drug name
HCl	hydrochloric acid or hydrochloride	Mistaken as potassium chloride (The "H" is misinterpreted as "K")	Use complete drug name unless expressed as a salt of a drug
HCT	hydrocortisone	Mistaken as hydrochlorothiazide	Use complete drug name
HCTZ	hydrochlorothiazide	Mistaken as hydrocortisone (seen as HCT250 mg)	Use complete drug name
MgSO4**	magnesium sulfate	Mistaken as morphine sulfate	Use complete drug name
MS, MSO4**	morphine sulfate	Mistaken as magnesium sulfate	Use complete drug name
MTX	methotrexate	Mistaken as mitoxantrone	Use complete drug name
PCA	procainamide	Mistaken as patient controlled analgesia	Use complete drug name
PTU	propylthiouracil	Mistaken as mercaptopurine	Use complete drug name
T3	Tylenol with codeine No. 3	Mistaken as liothyronine	Use complete drug name
TAC	triamcinolone	Mistaken as tetracaine, Adrenalin, cocaine	Use complete drug name
TNK	TNKase	Mistaken as "TPA"	Use complete drug name
ZnSO4	zinc sulfate	Mistaken as morphine sulfate	Use complete drug name

Stemmed Drug Names	Intended Meaning	Misinterpretation	Correction
"Nitro" drip	nitroglycerin infusion	Mistaken as sodium nitroprusside infusion	Use complete drug name
"Norflox"	norfloxacin	Mistaken as Norflex	Use complete drug name
"IV Vanc"	intravenous vancomycin	Mistaken as Invanz	Use complete drug name

Symbols	Intended Meaning	Misinterpretation	Correction
ʒ ♏	Dram Minim	Symbol for dram mistaken as "3" Symbol for minim mistaken as "mL"	Use the metric system
x3d	For three days	Mistaken as "3 doses"	Use "for three days"
> and <	Greater than and less than	Mistaken as opposite of intended; mistakenly use incorrect symbol; "< 10" mistaken as "40"	Use "greater than" or "less than"
/ (slash mark)	Separates two doses or indicates "per"	Mistaken as the number 1 (e.g., "25 units/10 units" misread as "25 units and 110" units)	Use "per" rather than a slash mark to separate doses
@	At	Mistaken as "2"	Use "at"
&	And	Mistaken as "2"	Use "and"
+	Plus or and	Mistaken as "4"	Use "and"
°	Hour	Mistaken as a zero (e.g., q2° seen as q 20)	Use "hr," "h," or "hour"

© ISMP 2007

**These abbreviations are included on TJC's "minimum list" of dangerous abbreviations, acronyms and symbols that must be included on an organization's "Do Not Use" list, effective January 1, 2004. Visit www.jointcommission.org for more information about this TJC requirement.

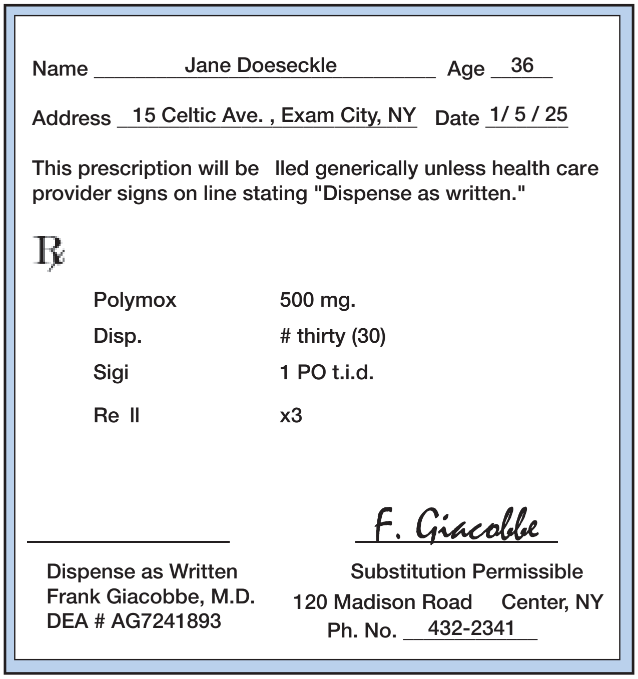
Permission is granted to reproduce material for internal newsletters or communications with proper attribution. Other reproduction is prohibited without written permission. Unless noted, reports were received through the USP-ISMP Medication Errors Reporting Program (MERP). Report actual and potential medication errors to the MERP via the web at www.ismp.org or by calling 1-800-FAIL-SAF(E). ISMP guarantees confidentiality of information received and respects reporters' wishes as to the level of detail included in publications.

Institute for Safe Medication Practices
www.ismp.org

Figure 5-1 Continued

If you are the medical assistant or nurse calling in the prescription to the facility for the physician, be sure to *repeat the name of the drug, dosage, frequency, and route of administration* to the physician as you write it on the patient's office record, adding the time the call was made and the name of the nurse receiving the call in the facility. This documentation is extremely important in preventing medication errors and legal complications. All TOs must be followed by a read-back statement; for example, "TO/RB" means it was a telephone order that was read back for accuracy. The physician must usually sign all VOs and TOs within 24 hours; refer to your institution's policy.

Medication orders can be written on the patient's record in the physician's office, clinic, or institution, or on a prescription blank (Figure 5-2). With the widespread use of electronic patient records in physicians' offices, prescriptions are typed into the system, printed out, and signed or sent directly to the pharmacy. This is referred to as **computerized physician order entry (CPOE)**. In the inpatient setting, **e-prescribing (eRx)** is the way medications are ordered through the electronic health record. The **electronic medication administration record (eMAR)** (Figure 5-3) is how administered medications are electronically recorded in the patient's health record.



Name Jane Doeseckle Age 36

Address 15 Celtic Ave. , Exam City, NY Date 1/ 5 / 25

This prescription will be filled generically unless health care provider signs on line stating "Dispense as written."

℞

Polymox	500 mg.
Disp.	# thirty (30)
Sigi	1 PO t.i.d.
Refill	x3

F. Giacobbe

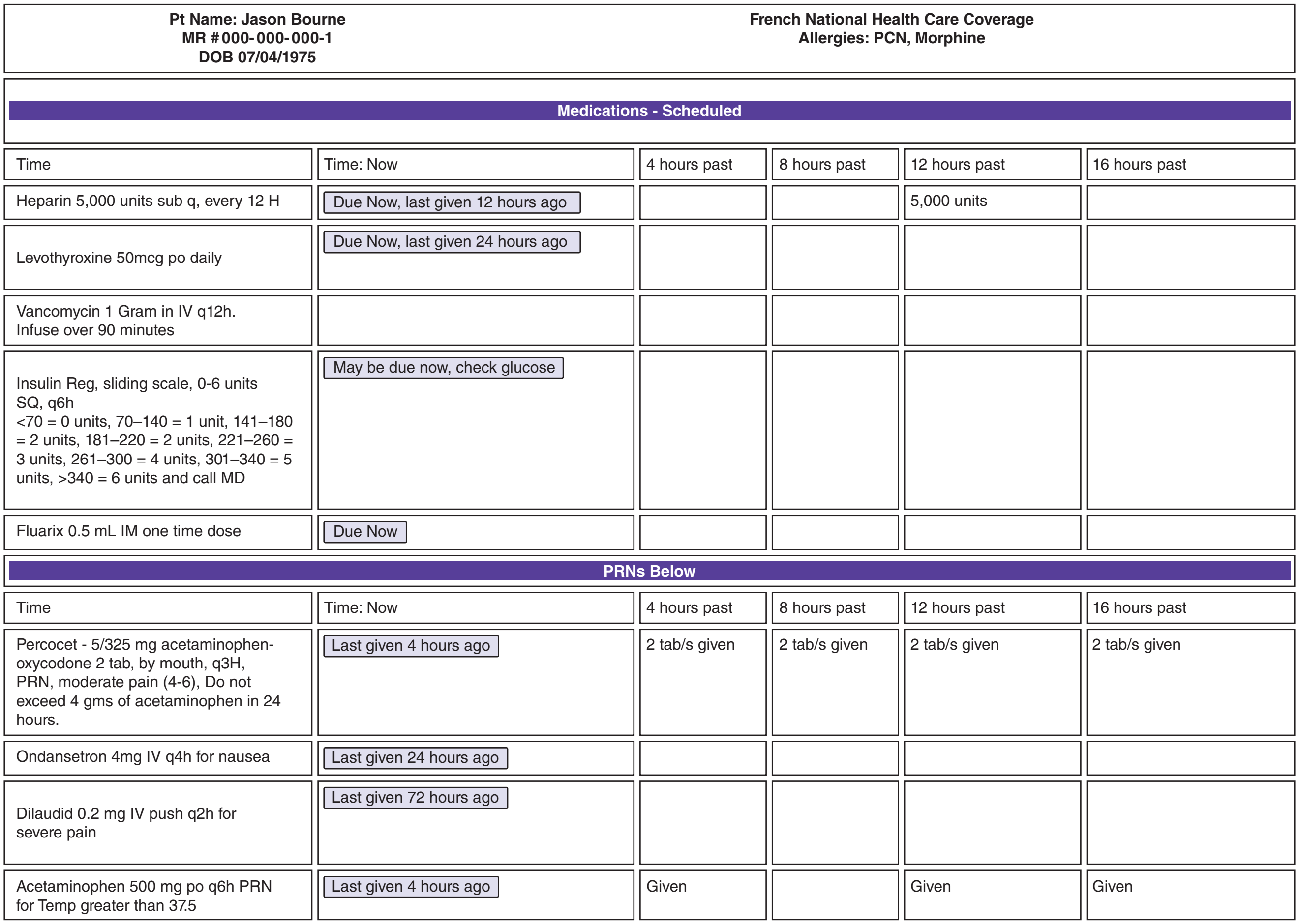
Dispense as Written
Frank Giacobbe, M.D.
DEA # AG7241893

Substitution Permissible
120 Madison Road Center, NY
Ph. No. 432-2341

Figure 5-2 Prescription blank. Check for completeness, legibility, and accuracy, including date, patient's name, medication name, dosage, route, frequency or time, number of refills, and the physician's Drug Enforcement Administration (DEA) number for controlled substances. Prescriptions may be printed, phoned, faxed, or sent electronically to the pharmacy.

It is the responsibility of the health care professional to check the medication order for completeness by noting the six items—date, patient's name, medication name, dosage, route, and frequency (plus additional items if using the prescription blank)—and to question any discrepancy, omission, or unusual order. The prescription blank contains two additional items: the physician's Drug Enforcement Administration registration number if the medication is a controlled substance and the number of times that the prescription can be refilled. If there are to be no refills, write the word *NO*, *NONE*, or *0* after Refill. Never leave a blank space in that area on the prescription blank.

To reduce the incidence of medication errors due to misinterpretation of the prescription, some states have passed legislation requiring the *name of the medication to be legibly printed or typed*. In addition, these regulations require the *quantity of the* *drug prescribed to be in both textual and numerical formats*, for example, "ten (10)." *The prescriber must also print their name under the signature* (Figure 5-2).



Pt Name: Jason Bourne
MR #000-000-000-1
DOB 07/04/1975

French National Health Care Coverage
Allergies: PCN, Morphine

Medications - Scheduled

Time	Time: Now	4 hours past	8 hours past	12 hours past	16 hours past
Heparin 5,000 units sub q, every 12 H	Due Now, last given 12 hours ago			5,000 units	
Levothyroxine 50mcg po daily	Due Now, last given 24 hours ago				
Vancomycin 1 Gram in IV q12h. Infuse over 90 minutes					
Insulin Reg, sliding scale, 0-6 units SQ, q6h <70 = 0 units, 70–140 = 1 unit, 141–180 = 2 units, 181–220 = 2 units, 221–260 = 3 units, 261–300 = 4 units, 301–340 = 5 units, >340 = 6 units and call MD	May be due now, check glucose				
Fluarix 0.5 mL IM one time dose	Due Now				

PRNs Below

Time	Time: Now	4 hours past	8 hours past	12 hours past	16 hours past
Percocet - 5/325 mg acetaminophen-oxycodone 2 tab, by mouth, q3H, PRN, moderate pain (4-6), Do not exceed 4 gms of acetaminophen in 24 hours.	Last given 4 hours ago	2 tab/s given	2 tab/s given	2 tab/s given	2 tab/s given
Ondansetron 4mg IV q4h for nausea	Last given 24 hours ago				
Dilaudid 0.2 mg IV push q2h for severe pain	Last given 72 hours ago				
Acetaminophen 500 mg po q6h PRN for Temp greater than 37.5	Last given 4 hours ago	Given		Given	Given

Figure 5-3 A screenshot of an EMARs. Notice the various medical abbreviations and units used in each order.

Systems of Measurement

To carry out a medication order accurately, the person administering medications must understand the different systems of measurement. The original system of weights and measures for writing medication orders was the *apothecary system*. An apothecary is a pharmacist or druggist. The apothecary system has now become obsolete. The **metric system** is the preferred system of measurement and is used at the present time. The third system of measurement is the **household system**, which is the least accurate. However, this system is more familiar to the layperson and therefore may be used in prescribing medications for the patient at home, or for over-the-counter (OTC) medications. A health care professional must understand systems of measurement and be able to convert from one system to another for accurate administration of medicines and for patient education. Medication orders are concerned with only two types of measurement: (1) measuring fluids, or liquid measure, and (2) measuring solids, or solid weight. It is helpful to keep in mind that the dosage of medication is delivered in a liquid, solid, or inhaled formula.

Metric System

The metric system was invented by the French in the late eighteenth century and is the international standard for weights and measures. It is based on three basic units of measure: the liter (L) for volume, the meter (m) for length, and the gram (g) for weight. A prefix representing a power of 10 can be placed before each of these basic units to change its value. For example, the prefix *milli* means "one thousandth," and therefore a milligram (mg) would be one thousandth of a gram. Another way of stating this is that 1,000 milligrams equal 1 gram.

Note

The milliliter (mL) is approximately equivalent to the cubic centimeter (cc). Therefore, 1 mL or milliliter is equal to 1 cc or cubic centimeter. However, it is preferred to *not* use the cc designation, as it is on the error-prone list.

The metric system is based on powers of 10. Therefore, understanding the powers of 10 is helpful to understand the basis of the metric system. While it may seem like a lot of math to go over exponents, this may help you reach a point where if you have to do a conversion between two metric units you will simply move the decimal point without any unnecessary calculations. Let's review some terminology first. Consider the expression b^n, where b is called the **base** and n is the **exponent**. The n represents the number of times that b is multiplied by itself. Refer to Figure 5-4.

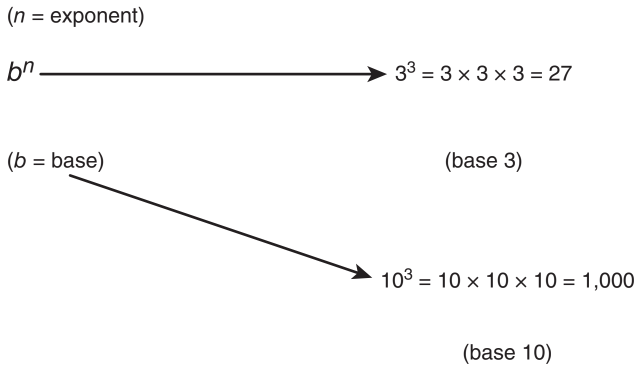


Figure 5-4 The exponential expression.

If we use 10 as the base, we can develop an exponential representation of the powers of 10 as follows:

$10^0 = 1$ (mathematically, any number that has an exponent of $0 = 1$)

$10^1 = 10$

$10^2 = 10 \times 10 = 100$

$10^3 = 10 \times 10 \times 10 = 1{,}000$

$10^4 = 10 \times 10 \times 10 \times 10 = 10{,}000$

$10^5 = 10 \times 10 \times 10 \times 10 \times 10 = 100{,}000$

$10^6 = 10 \times 10 \times 10 \times 10 \times 10 \times 10 = 1{,}000{,}000$

This also works for smaller numbers that are less than 1. For these we use negative exponents. Here is an example:

$10^{-1} = 1/10 = 0.1$

$10^{-2} = 1/10 \times 1/10 = 0.01$

$10^{-3} = 1/10 \times 1/10 \times 1/10 = 0.001$

$10^{-4} = 1/10 \times 1/10 \times 1/10 \times 1/10 = 0.0001$

$10^{-5} = 1/10 \times 1/10 \times 1/10 \times 1/10 \times 1/10 = 0.00001$

$10^{-6} = 1/10 \times 1/10 \times 1/10 \times 1/10 \times 1/10 \times 1/10 = 0.000001$

Because all metric prefixes are based on the powers of 10, to convert within the metric system, you simply need to move the decimal point to the correct number of places of the power of 10 that the prefix represents. Table 5-2 shows the most common prefixes in the metric system.

Table 5-2 Metric Equivalents for Solid (Grams) and Liquid (Liters) Measurement

Metric (Grams)	Metric (Milligrams)	Metric (Micrograms)
1 g	1,000 mg	1,000,000 mcg
0.1 g	100 mg	100,000 mcg
0.001 g	1 mg	1,000 mcg
0.000001 g	0.001 mg	1 mcg
Metric (Liters)	**Metric (Milliliters)**	
1 L	1,000 mL	
0.5 L	500 mL	
0.1 L	100 mL	
0.05 L	50 mL	

Note: Micrograms are used for narrow therapeutic index drugs such as levothyroxine and digoxin. These medications have a very high potency and a very small range between when they are effective and when they become toxic and cause side effects; therefore, it is important to use micrograms to ensure a proper dose for each patient. Microliters are not commonly used in measurement.

When you understand the metric system, it is not necessary to memorize equivalents because knowing that *milli* represents one thousandth or, mathematically, multiplying by 0.001, you simply move the decimal point three places to the right when converting grams to milligrams or even liters to milliliters as shown in Table 5-3.

Table 5-3 Meaning of Metric System Prefixes

Thousands	Hundreds	Tens	Base Units	Tenths	Hundredths	Thousandths
Kilo-	Hecto-	Deca-	Liter, meter, or gram	Deci-	Centi-	Milli-
(k)	(h)	(da)	(l), (m), (g)	(d)	(c)	(m)
10^3	10^2	10^1	10^0 or 1	10^{-1}	10^{-2}	10^{-3}

The ease of working with the metric system is that to change from one prefix to another, you simply move the decimal point to the correct place. In other words, to convert within the system, simply move the decimal point for each power of 10 according to the desired prefix.

Let's look at an example: 50 kg (kilograms) is equal to how many grams? Again, knowing the prefixes and powers of 10 by referencing Table 5-3, we can move the decimal point 3 places (powers of 10) to the right to give the answer of 50,000 g (grams).

Learning Hint

To make this simpler and more practical to use, please use this simple system that allows you to easily convert between grams/liters, milligrams/milliliters, and micrograms/microliters, the types of conversions needed for drug dosages. Note that each box represents a power of 10 and you simply move the decimal the correct number of places and direction starting with your given unit. For example, 500,000 micrograms is equal to how many milligrams? Starting with 500,000 micrograms, you move the decimal point 3 places to the left to give you 500 milligrams. You can use this simple system for any conversion between these units of measure.

Grams or Liters	X	X	milli	x	x	micro

Each Box represents a power of 10.

Let's try another conversion going in the other direction. 1,500 mL is equivalent to how many liters? Now you are starting with mL and moving 3 places or powers of 10 to the left; therefore, the decimal moves 3 places to give you 1.5 liters.

Household System

At times it may be necessary to convert a dosage from the metric system to the household system, especially in the home care setting. It is important to have access to the few basic equivalents most commonly used. Table 5-4 lists commonly used approximate equivalents for liquid measurement. If it is necessary to convert from one system of measurement to another, always consult a conversion table or a pharmacist to avoid dangerous errors.

Table 5-4 Common *Approximate* Equivalents for Liquid Measurement

Metric	Household
5 mL	1 tsp
15 mL	1 tbsp
30 mL	1 oz
240 mL	1 measuring cup
473 mL	1 pt
946 mL	1 qt

Common Medical Conversion

Although almost all countries use the metric system as their official measurement system, the United States still uses the English system of measurement, which includes ounces, pounds, feet, miles, and yards. Often a **conversion of units** is needed to properly treat the patient. There is a method of converting English units to metric units and back called the **factor-label method**. This method lets your starting units cancel or divide out until you reach your desired unit. There are two steps. First, write your starting value with its unit as a fraction numerator over the number 1 as the denominator. Any fraction that contains 1 as the denominator is equal to the starting value. Next, place the units you started with in the denominator of a second fraction to divide or cancel out, and place the unit you want to convert to in the numerator, along with the corresponding equivalent values. The quantities in the numerator and denominator must be equivalent values in different units. Because the values are equivalent, this is the same as multiplying by 1, which does not change the value of the mathematical expression. This lets you treat the units as in the multiplication of fractions and "cancel" them out. Notice that by carefully placing the units so that canceling units is possible, the units can be converted.

Let's examine a simple nonmedical example of how units cancel.

How many seconds are in two (2) hours?

$$\frac{2\ \cancel{\text{hr}}}{1} \times \frac{60\ \text{min}}{1\ \cancel{\text{hr}}} = 120\ \text{minutes}$$

$$\frac{120\ \cancel{\text{min}}}{1} \times \frac{60\ \text{sec}}{1\ \cancel{\text{min}}} = 7{,}200\ \text{sec}$$

Here is a common medical example: A patient weighs 170 pounds and is ordered a drug dosage of 10 mg/kg. You need to calculate how much of the drug they should receive. You need to change the pounds to kilograms, so write the given weight over the denominator of 1. Then place the unit you want to cancel (pounds) in the denominator and the unit you want to convert (kilograms) in the numerator of the second fraction.

$$\frac{170\ \cancel{\text{lb}}}{1} \times \frac{1\ \text{kg}}{2.2\ \cancel{\text{lb}}} = 77.27\ \text{kg}$$

Because the dose reads 10 mg/kg, this patient should receive 10 × 77.27 mg, or 772.7 mg of the prescribed medication. You may need to round, depending on the medication units available.

Warning: Be very careful in calculating the weight in kilograms. The slightest error, especially in pediatric doses, could result in serious or fatal consequences. It is very important to commit to memory that to convert pounds to kilograms, you divide the number of pounds by 2.2.

Clinical Application

You may notice medications ordered in international units (IU) or milliequivalents. Do not let these units confuse you. Treat them the same as you would any unit label such as "mgs." IU is a measure that refers to the amount of substance contained in a medication or the strength of the medication. Typically, IUs are used for heparin, insulin, vitamins, enzymes, and vaccines.

Milliequivalent (mEq) is similar to an IU, as it describes the amount of substance dissolved in another. This term is often used in lab results and when prescribing certain electrolyte replacements such as potassium chloride. No calculations are needed because the dosages and values are individualized.

Patient Education

When explaining dosage preparation, always speak directly to the patient and observe the patient for comprehension. Many older patients may have difficulty hearing but may be reluctant to admit lack of understanding. Ask them to repeat the directions.

Many older patients may also have vision problems. Be sure the directions for dosage preparation are written clearly. If a family member will be assisting in the preparation and administration of medications, include that person in the instruction. Be sure that any measuring equipment to be used is clearly marked.

Measuring spoons and clearly marked measuring cups should be used when available for household measurement. Such calibrated utensils are more accurate than tableware (Figure 5-5). Teaspoons, tablespoons, teacups, and drinking glasses vary in size and capacity, and therefore measurements using such utensils are inaccurate.

Thammasak Lek/Shutterstock.com.

Figure 5-5 For accurate household measurement, standard measuring spoons are used versus common utensil spoons.

Chapter Review Quiz

Interpret the following orders

1. Keflex 250-mg cap PO q6h

______________________________.

2. Neosporin ophth sol 2 gtt in OU tid

______________________________.

3. Feosol 65-mg tab bid pc c̄ orange juice

______________________________.

4. Diuril 500 mg PO qAM

______________________________.

5. Dyazide 1 cap bid

______________________________.

6. Demerol 50 mg IM q4h PRN for pain

______________________________.

7. Metamucil 1tsp mixed c̄ 8oz H_2O bid pc

____.

8. Dulcolax supp R PRN for constipation

____.

9. Robitussin syr 1tsp q4h PRN for cough

____.

10. Nitrostat 1 tab SL PRN for angina attack, may repeat q5min three times

____.

11. Phenergan supp 25 mg PRN q6h for nausea

____.

12. Discontinue Phenergan 48h postop

____.

13. Glipizide 5 mg PO daily c̄ breakfast

____.

14. Cefazolin 1 g IVPB q8h

____.

15. Potassium chloride 20 mEq in NS 1L IV to run at 80 mL per hour

____.

16. NPH Insulin 20 units subcu daily ac breakfast

____.

17. Glyburide 2.5 mg daily c̄ breakfast

____.

18. Gentamicin ophth sol 1 gtt q3h OD

____

19. Cefaclor suspension 20 mg/kg/day in two equal doses q12h

____

20. Ambien 5 mg for sleep PRN, may repeat once PRN

____.

21. Which of the following is the oldest system of measurement for medication?

a. household
b. metric
c. apothecary
d. English

22. Which of the following is true regarding telephone orders?

a. Always read back and verify accuracy.
b. Anyone can accept a telephone order.
c. The physician does not need to sign the order later.
d. Under no circumstances can telephone orders be used.

23. Which of the following is not part of a medication order?

a. date/time that the order was taken

b. patient's name

c. medication name

d. dosage and/or amount of medication

e. which pharmacy to use

24. When teaching a patient to administer medications at home, which of the following would you instruct them to use to deliver 1 tsp of a liquid medication?

a. a soup spoon

b. a medication cup with marked lines

c. a cup

d. a measuring spoon for cooking

Complete the following conversions and place the correct answer in the blank

25. 1,000 mg = ___ g

26. 75 mg = ___ g

27. 1 kg = ___ lb

28. 150 lb = ___ kg

29. 1 tsp = ___ mL

30. 1 tbsp = ___ mL

31. 100 kg = ___ lb

32. 0.5 g = ___ mg

33. 1 g = ___ mg

34. 100 mcg = ___ mg

35. A 6-month-old child is brought to the pediatrician's office by their parent for evaluation of a fever and fussiness. You obtain a set of vital signs and a weight of 17.6 pounds. The physician determines that the child has otitis media (an ear infection). They order the antibiotic cephalexin 15 mg/kg PO qid for 7 days. How many milligrams of medication should the patient receive per dose?

Chapter 6

Safe Dosage Calculations

Key Terms and Concepts

Calculating dosage
Clark's Rule
Denominator
Mixed number
Numerator
Proportion
Ratio
Unit-dose form
Verify your calculations
Young's Rule

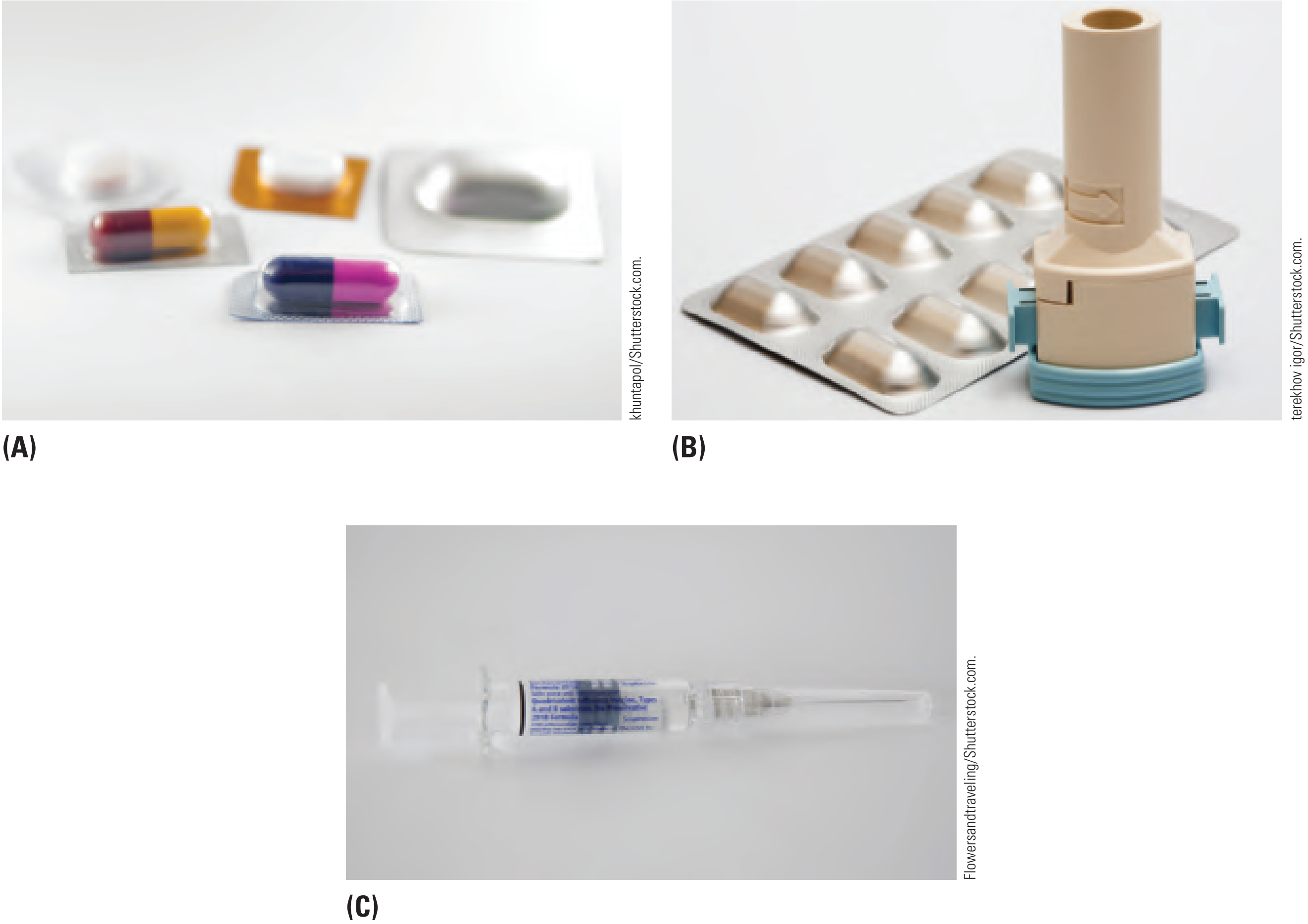
Objectives

Upon completion of this chapter, the learner should be able to:

1. Review basic functions of a calculator.
2. Calculate arithmetic problems using fractions, decimals, percentages, ratios, and proportions.
3. Solve dosage problems using the basic calculation method.
4. Solve dosage problems using the ratio and proportion method.
5. List the cautions with the basic calculation method.
6. List the cautions with the ratio and proportion method.
7. Calculate safe dosages for infants and children.
8. List the variables when assessing geriatric patients for safe dosage.
9. List five steps to reduce medication errors.

"First, do no harm." Health care professionals are dedicated to the principle of helping others, not harming them. Nowhere is this principle more important than in the calculation, preparation, and administration of safe dosages. One careless mistake can lead to a catastrophe. It is the responsibility of the health care professional to be absolutely certain that the medication administered is exactly as prescribed by the physician, *and* is also an *appropriate* dose for that particular patient. Doses for children and older adults can vary significantly from the average dose. Therefore, it may be necessary to calculate a partial dose from the dose on hand for the average patient.

Many medications are dispensed by the pharmacist in **unit-dose form** (Figure 6-1), in which each individual dose of medicine is prepackaged in a separate packet, vial, or prefilled syringe. Although much of the mixing and measuring of medications is now completed by the pharmacist, the person who is administering medications must understand the preparation of dosages to ensure accuracy. On occasion the dosage



khuntapol/Shutterstock.com.

terekhov igor/Shutterstock.com.

Flowersandtraveling/Shutterstock.com.

Figure 6-1 Examples of unit-dose medications. (A) Unit-dose oral medications. (B) Unit-dose capsules for dry powder inhalation device. (C) Prefilled unit-dose syringe for injection.

ordered differs from the dose on hand. Consequently, it may be necessary to calculate the correct dosage. Calculations can be a simple procedure if you follow the necessary steps in sequential order.

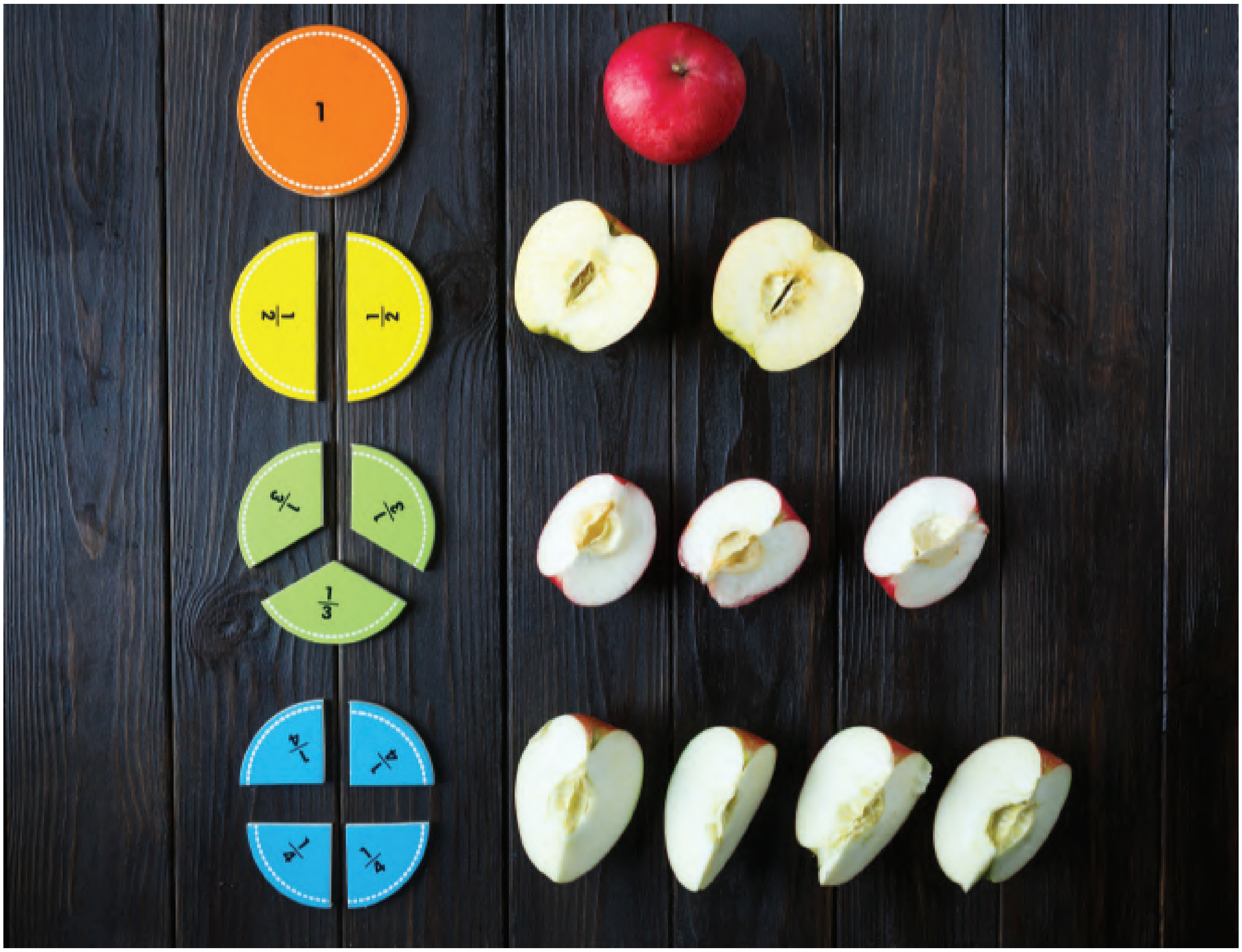
A working knowledge of basic arithmetic is required for accurate calculation of drug dosages. You need to be able to use a calculator and to perform basic arithmetic, including addition, subtraction, multiplication, division, decimals, fractions, and percentages. We will start with a basic calculator overview, followed by a math review. Even though the calculator review may seem simple, teachers often find students who set up the problem correctly but make simple calculator entry errors.

Using a Calculator

Basic function keys on a calculator include addition (+) subtraction (−), multiplication (* or ×), division (/ or ÷), and total (=); to clear, use the (C) key. After you enter any number in the calculator, review it to make sure you entered the correct number. When you get an answer, it is a good idea to repeat the calculation and make sure you get the same answer; if not, you may have entered something wrong. Lastly, have an estimate in your mind to verify that your answer is reasonable. For example, you would not expect to ever give 100 pills, so if you get an answer of 100 pills, you should redo the math.

Fractions

The top number of a fraction is called the **numerator** and it stands for how many parts of the whole exist in the fraction. The bottom number of the fraction is the **denominator**, how many equal parts the whole is divided into. Refer to Figure 6-2.



Chekyravaa/Shutterstock.com.

Figure 6-2 Examples of fractions using apples.

Learning Hint

Mixed Numbers

You may encounter mixed numbers in your practice. A **mixed number** is a whole number and a fraction. For example, someone may need $1\frac{1}{2}$ pills. If you need to perform calculations, you will need to change mixed numbers (e.g., $1\frac{1}{2}$) to improper fractions. To do this, you multiply the whole number by the denominator, add the product to the numerator, and place the sum over the denominator (3/2).

To add and subtract fractions, remember that the fractions must have the same denominator. You simply add or subtract the numerators and leave each denominator the same.

Examples:

$$\frac{1}{3} + \frac{1}{3} = \frac{2}{3}$$

$$\frac{7}{8} - \frac{2}{8} = \frac{5}{8}$$

If you need to add or subtract fractions with different denominators, you need to find a common denominator.
Example:

$$\frac{1}{6} + \frac{1}{5}$$

The common denominator is 30 because both 6 and 5 are multiples of 30.

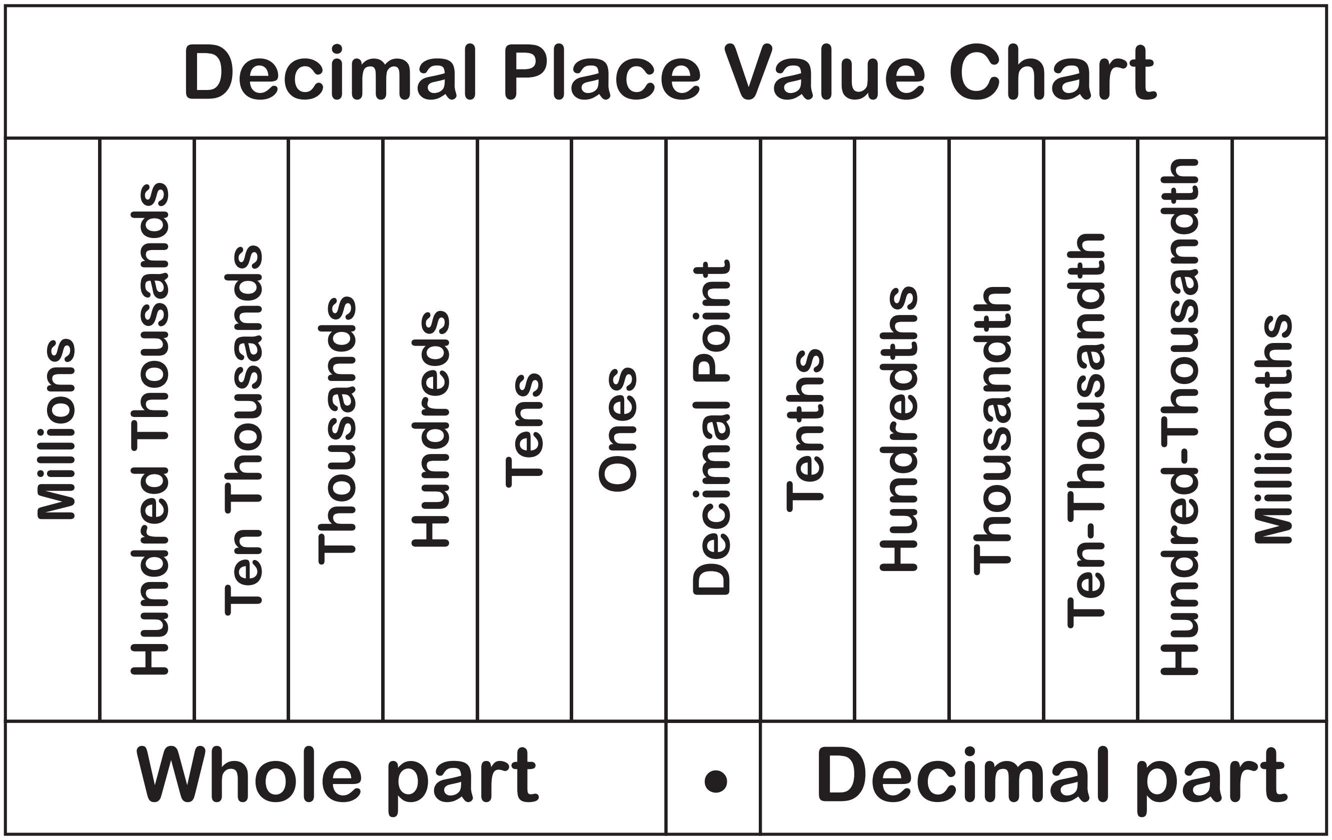
$$\frac{1}{6} \times \frac{5}{5} = \frac{5}{30}$$

$$\frac{1}{5} \times \frac{6}{6} = \frac{6}{30}$$

$$\frac{5}{30} + \frac{6}{30} = \frac{11}{30}$$

Decimals

Decimals are very similar to fractions. You can change fractions to decimals and decimals to fractions. Figure 6-3 is a review of how the decimal system works.



Decimal Place Value Chart

Millions	Hundred Thousands	Ten Thousands	Thousands	Hundreds	Tens	Ones	Decimal Point	Tenths	Hundredths	Thousandth	Ten-Thousandth	Hundred-Thousandth	Millionths
Whole part							•	Decimal part					

zizou7/Shutterstock.com.

Figure 6-3 Decimal place value chart.

Rounding decimals is important for administering the correct dosage. For example, tablets often come with a score line so that you can easily give 0.5 of a tablet. If, for example, your calculation came to 1.48 tablets, you would round up and give 1.5 tablets. When working with liquids you would use a syringe and give the exact tenth of a dosage. Whenever you need to add, subtract, multiply, or divide decimals you should use your calculator. Additionally, understand that dosages will be calculated by the pharmacy in your EMAR, but you should always double-check the math and think critically.

Percentages

Percent is a number over the denominator of 100. When thinking of percents, decimals, and fractions it is sometimes helpful to think about the U.S. currency system (money).

The basis of the currency system is \$1.

$$\text{A quarter} = 25 \text{ cents} = 0.25 \text{ (decimal form)} = \frac{25}{100} \text{ (fractional form)} = 25\%$$

$$\text{A dime} = 10 \text{ cents} = 0.10 = \frac{10}{100} = 10\%$$

To convert from percent to decimal, move the decimal point two places to the left since you are multiplying by 0.01.

$$25\% = 0.25$$

Clinical Application

Patients are often placed on supplemental oxygen, and this is ordered as a fractional inspired amount of oxygen abbreviated FIO_2. A patient who is ordered an oxygen mask at an FIO_2 of 0.50 would be getting $\frac{50}{100}$ or 50% oxygen. Our normal atmosphere, or what we normally breathe, is 0.21 or 21% oxygen.

jomphong/Shutterstock.com.

Ratios and Proportions

Ratios and proportions are used in health care and medicine as a way to compare measurements. Health care professionals use ratios and proportions to solve a variety of equations and make comparisons between unlike items. A **ratio** is a comparison of numbers by division. Recipes for cooking and baking use ratios all the time. For example, imagine you are making oatmeal for breakfast. The recipe calls for two cups of liquid (milk, almond milk, or water) for every one cup of dry oats. This is a ratio of 2:1. If you wanted to make more oatmeal or less oatmeal, you would adjust the ratio accordingly. If you wanted to double the oatmeal, you would use four cups of liquid to two cups of dry oats. If you wanted to cut the recipe in half, you would use one cup of water and one-half cup of dry oats. An example in health care is when medication is ordered in mg per kg. We use a ratio to increase or decrease the dosage based on the weight of the patient. Ratios work in a way that is very similar to fractions.

A **proportion** is an equation which states that two ratios are equal. Proportions are typically set up like this:

$$\frac{1}{2} = \frac{2}{4}$$

You will be finding an unknown value in a proportion when you complete a dosage calculation. Here are the steps to solving a proportion with an unknown variable. It is called cross multiplication.

- Set the cross products equal to each other to form an equation.
- Isolate the variable on one side of the equation by dividing both sides by the number that is multiplied by that variable.
- Check by substituting the result into the original proportion and finding the cross products.

Example:

$$\frac{4}{2} = \frac{n}{3}$$

Cross multiplying yields:

$$12 = 2n$$

Divide both sides by 2:

$$n = 6$$

Remember to keep like measures together on both sides. It doesn't matter, numerator or denominator, as long as they are the same on both sides of the equals sign. We will use ratios and proportions in upcoming sections of this chapter to calculate medication dosages.

Calculation Guidelines

Remember, there is no margin of error when administering medications. It is possible for a small error in arithmetic to seriously harm a patient. A misplaced decimal point could cause a fatality. Safe dosage preparation requires (1) a working knowledge of basic arithmetic and (2) meticulous care with all calculations.

Calculations can be as simple as 1, 2, 3. When the dosage ordered differs from the dose on hand, the problem can be solved simply by completing three basic steps:

1. Check whether all measures are in the same system. If necessary, convert by using known conversion factors or use the ratio and proportion method.
2. Write the problem in equation form, *using the appropriate formula and labeling all parts,* and complete the necessary calculations.
3. *Check the accuracy* of your answer for reasonableness and have someone else **verify your calculations**.

There are several different methods of **calculating dosage**. Either of the methods presented in this text may be used, or both methods may be used to verify accuracy. The two methods presented here are *basic calculation* and *ratio and proportion*. Basic calculation requires only simple arithmetic; ratio and proportion requires the ability to determine an unknown, *X*.

Method 1: Basic Calculation

Use the following formula:

$$\frac{\text{desired dose}}{\text{on-hand dose}} \times \text{quantity of on-hand dose}$$

In short form:

$$\frac{D}{OH} \times Q$$

Example 1

The physician orders 162 mg of aspirin q4h PRN for fever over 101°. On hand are aspirin 81-mg tablets. How many tablets do you give your patient per dose?

Step 1. Check whether all measures are in the same system. No conversion is necessary. Both measures are in milligrams.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{162 \text{ mg}}{81 \text{ mg}} \times 1 \text{ tab} = 162 \div 81 = 2 \text{ tabs}$$

Note: The unit labels of the desired and on-hand doses must be the same. The unit label of the answer must be the same as the quantity.

Step 3. Check for reasonableness. A drug reference source should be checked to confirm this is a reasonable dosage.

If the calculations resulted in an answer such as ¼ tablet or 5 tablets, the answer may not be reasonable and the calculations should be rechecked. If calculations are correct after recheck, any unusual dosage should be checked with the person in charge: the pharmacist or the physician. *When in doubt, always question.*

Example 2

The narcotics drawer contains vials of meperidine (Demerol) labeled 75 mg in 1 mL. The preoperative order reads Demerol 60 mg IM on call. How many milliliters do you give your patient?

Step 1. Check whether all measures are in the same system. No conversion is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{60\text{ mg}}{75\text{ mg}} \times 1\text{ mL} =$$

Reduce fractions to lowest terms:

$$\frac{60}{75} = \frac{12}{15} = \frac{4}{5}$$

Convert fractions to decimals:

$$\frac{4}{5} = 5\overline{)4.0}^{\,0.8}$$

Multiply by quantity:

$$0.8 \times 1\text{ mL} = 0.8\text{ mL}$$

Note: Fractions must be converted to decimals and rounded off to one decimal place to coincide with the markings on the syringe.

Step 3. Check for reasonableness. A dose of 0.8 mL is within the normal dosage range. It also makes sense that if you have 75 mg in 1 mL dose on hand and the order is to deliver 60 mg, you would have to give less than 1 mL of your dose on hand.

Example 3

The physician orders midazolam (Versed) 3 mg IM preoperatively. On hand are vials labeled 5 mg per mL. How many milliliters do you deliver?

Step 1. Check to see if all measures are in the same system.
No conversion is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{3\text{ mg}}{5\text{ mg}} \times 1\text{ mL} = 3 \div 5 = 5\overline{)3.0}^{\,0.6}$$

$$0.6 \times 1\text{ mL} = 0.6\text{ mL}$$

Step 3. Check for reasonableness. A dose of 0.6 mL is within the normal dosage range.

Example 4

The order reads atropine sulfate 0.6 mg IM on call to surgery. Available ampules are labeled atropine sulfate $\frac{0.4\text{ mg}}{\text{mL}}$. How many milliliters do you give your patient?

Step 1. Check whether all measures are in the same system.
No conversion is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

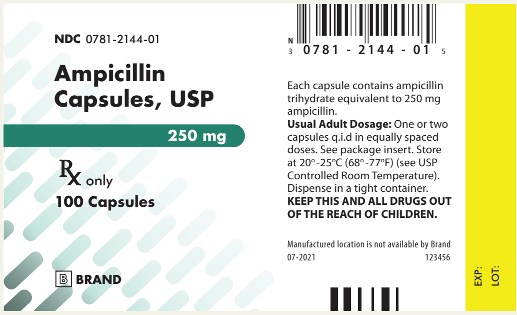
$$\frac{0.6\text{ mg}}{0.4\text{ mg}} \times 1\text{ mL} = 0.6 \div 0.4 = 0.4\overline{)0.6}^{\,1.5}$$

$$1.5 \times 1\text{ mL} = 1.5\text{ mL}$$

Step 3. Check for reasonableness. A dose of 1.5 mL is within the normal dosage range.

Example 5

This example is going to combine reading the medication label and conversions within the metric system. The order reads ampicillin 0.5 g. This is the available medication label:



NDC 0781-2144-01

Ampicillin Capsules, USP

250 mg

℞ only

100 Capsules

BRAND

N 3 0781 - 2144 - 01 5

Each capsule contains ampicillin trihydrate equivalent to 250 mg ampicillin.
Usual Adult Dosage: One or two capsules q.i.d in equally spaced doses. See package insert. Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature). Dispense in a tight container.
KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Manufactured location is not available by Brand
07-2021 123456

EXP:
LOT:

How many capsules do you give your patient?

Step 1. Check whether all measures are in the same system. Convert grams to milligrams either or by moving the decimal point 3 places to the right, or mathematically as follows:

$$1 \text{ g} = 1{,}000 \text{ mg}$$

$$0.5 \text{ g} = 0.5 \times 1{,}000 = 500 \text{ mg}$$

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{500 \text{ mg}}{250 \text{ mg}} \times 1 \text{ cap} =$$

Reduce fractions to lowest terms:

$$\frac{500}{250} = 50 \div 25 = 2$$

$$2 \times 1 = 2 \text{ caps}$$

Step 3. Check for reasonableness. A dose of 2 caps, or 500 mg, is within the normal dosage range.

Cautions for the basic calculation method:

1. *Label* all parts of the formula.
2. Use the *same unit label* for desired and on-hand doses.
3. Use the *same unit label* for the quantity and the answer (the amount to be given).
4. *Reduce fractions* to lowest terms before dividing.
5. Multiply by the quantity after dividing.
6. Take extra care with decimals.
7. *Convert* fractions to decimals.
8. *Round off* decimals to one decimal place after computation is complete.
9. *Verify the accuracy* of calculations with an instructor.
10. Question the answer if it is not within normal limits (e.g., less than ½ tab, more than 2 tabs, or more than 2 mL for injection).

Method 2: Ratio and Proportion

Earlier in the chapter we discussed ratios and proportions. Now we will apply that knowledge to solving dosage calculations. There are three basic steps to using the ratio and proportion method.

Step 1. Set up a proportion of the dose on hand and the desired dose.
Step 2. Make sure all units are equal.
Step 3. Cross multiply to solve the equation.

Refer to Figure 6-4.

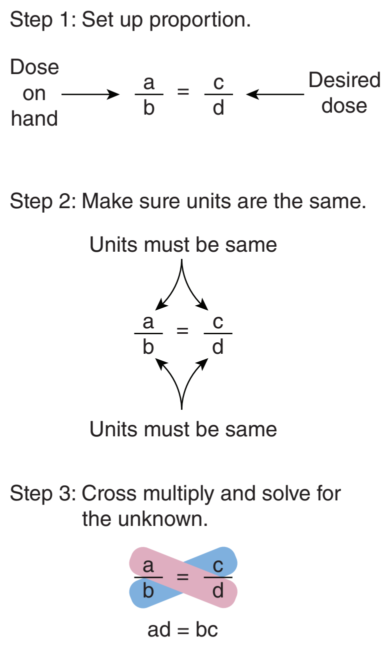

Step 1: Set up proportion.
Dose on hand
a/b = c/d
Desired dose
Step 2: Make sure units are the same.
Units must be same
a/b = c/d
Units must be same
Step 3: Cross multiply and solve for the unknown.
a/b = c/d
ad = bc

Figure 6-4 Ratio and Proportion method.

Example 1

The preoperative order reads Demerol 60 mg IM on call. The narcotics drawer contains vials labeled meperidine (Demerol) $\frac{100 \text{ mg}}{2 \text{ mL}}$. How many milliliters would you give?

Step 1. Verify that all measures are in the same system.

No conversion is necessary.

Step 2. Set up the problem as a ratio and label all terms:

$$\text{(dose on hand) } \frac{100 \text{ mg}}{2 \text{ mL}} = \frac{60 \text{ mg}}{X \text{ mL}} \text{ (desired dose)}$$

Step 3. Cross multiply.

$$100X = 120$$

Divide both sides by 100 to isolate the unknown variable (X).

$$\frac{100X}{100} = \frac{120}{100}$$

$$X = 1.2 \text{ mL}$$

Step 4. Check for reasonableness. A dose of 1.2 mL is within the normal dosage range.

Example 2

Meperidine oral solution is available as Demerol solution 50 mg/5 mL. The order reads Demerol liquid 150 mg PO q6h PRN. How many milliliters would you give?

Step 1. Verify that all measures are in the same system.

No conversion is necessary.

Step 2. Set up the problem as a ratio and label all terms:

$$\frac{50\text{ mg}}{5\text{ mL}} = \frac{150\text{ mg}}{X\text{ mL}}$$

Step 3. Cross multiply.

$$50X = 750$$

$$\frac{50\text{ mg}}{5\text{ mL}} = \frac{150\text{ mg}}{X\text{ mL}}$$

$$X = 15\text{ mL}$$

Step 4. Check for reasonableness. An oral dose of 15 mL is appropriate for an adult.

Example 3

Now we will evaluate an example where you will need to convert from one system of measure to another.

The physician is treating a 44-lb child for epilepsy. The order reads phenobarbital elixir 3 mg/kg at bedtime. Phenobarbital elixir is labeled 15 mg/5 mL. How many milliliters will the child receive?

Step 1. Verify that all measures are in the same system. Pounds (lb) must be converted to kilograms (kg). To convert lb to kg, divide the number of pounds by 2.2.

The child weighs 20 kg.

The order reads $\frac{3\text{ mg}}{\text{kg}}$. Therefore, $\frac{3\text{ mg}}{\cancel{\text{kg}}} \times 20\ \cancel{\text{kg}} =$ 60-mg dose.

Step 2. Set up the problem as a ratio. Label all terms:

$$\frac{15\text{ mg}}{5\text{ mL}} = \frac{60\text{ mg}}{X\text{ mL}}$$

Step 3. Cross multiply.

$$15X = 300$$

$$\frac{15X}{15} = \frac{300}{15}$$

$$X = 20\text{ mL}$$

Step 4. Check for reasonableness. An oral dose of 20 mL is a large amount for a young child to take at one time. The physician might want to divide the daily dose. If so, the order would be written: phenobarbital 30 mg BID.

Example 4

An 88-lb child with cancer has an order for pain medication that reads morphine liquid PO 0.2 mg/kg q4h PRN. Available morphine solution is labeled 20 mg/5 mL. How many milliliters would you give?

Step 1. Verify that all measures are in the same system. Pounds (lb) must be converted to kilograms (kg). To convert lb to kg, divide the number of pounds by 2.2.

The child weighs 40 kg.
The order reads 0.2 mg/kg. Therefore, $\frac{0.2\text{ mg}}{\cancel{\text{kg}}} \times 40\ \cancel{\text{kg}} = $ 8-mg dose.

Step 2. Set up the problem as a ratio. Label all terms:

$$\frac{20\text{ mg}}{5\text{ mL}} = \frac{8\text{ mg}}{X\text{ mL}}$$

Step 3. Cross multiply.

$$20X = 40$$

$$\frac{20X}{20} = \frac{40}{20}$$

$$X = 2\text{ mL}$$

Step 4. Check for reasonableness. When consulting a drug reference source, an oral dose of 2 mL is appropriate for a child who is diagnosed with cancer.

Example 5

The physician orders Benadryl elixir 25 mg q12h. The bottle in the medicine cupboard is labeled 12.5 mg/1 tsp. How many mL will you administer?

Step 1. Verify that all measures are in the same system. Convert tsp to mL. 1 tsp = 5 mL (either reference a chart or recall).

Step 2. Write the problem as a proportion and label each term:

$$\frac{12.5\text{ mg}}{5\text{ mL}} = \frac{25\text{ mg}}{X\text{ mL}}$$

Step 3. Cross multiply.

$$12.5X = 125$$

$$X = 10\text{ mL}$$

Step 4. Check for reasonableness. The dose 10 mL is within normal limits for oral solution.

Cautions for the Ratio and Proportion Method

1. *Label* all parts of the equation.
2. The ratio on the *left* contains the *known* quantity, and the ratio on the *right* contains the *desired* and *unknown* quantities.
3. Terms of the second ratio must be in the same sequence as those in the first ratio.
4. *Cross multiply and solve for the unknown.*
5. Take extra care with decimals.
6. *Convert* fractions to decimals. *Round off* decimals to one decimal place.
7. *Label* the answer.
8. *Verify the accuracy* of calculations with an instructor.
9. *Question* any unusual dosage that is not within normal limits (e.g., less than ½ tab, more than 2 tabs, or more than 2 mL for injection).

Pediatric Dosage

Children are not miniature adults. You cannot merely take a portion of an adult dose and give it to a child. There are many other variables to consider. There are numerous formulas available for computing an *approximate* child's dose based on body surface area, weight, or age. However, other factors must be taken into consideration as well. In neonates, renal function and some enzyme systems needed for drug absorption and metabolism are not fully developed. The neonate's blood–brain barrier is more permeable, and their total body water contributes to a greater percentage of body weight, also affecting drug absorption.

Appropriate dosage for children, as well as adults, must take into consideration variables such as age; weight; sex; and metabolic, pathological, or psychological conditions. Recommended pediatric drug dosages are derived from data obtained in clinical trials utilizing children who are sick. When preparing drug dosages for children, it is important to always refer to recommended dosages as listed in drug inserts, *Physicians' Desk Reference (PDR)*, or *AHFS (American Hospital Formulary Service) Drug Information (AHFS DI).*

Clinical Application

There are multiple methods used to calculate dosing for children, but the most common are Clark's Rule and Young's Rule. **Young's Rule** is based off the child's age in years and is useful for medications that have variations in dosing based on age. It is calculated using the following formula:

$$\frac{(\textit{child's age in years})}{(\textit{child's age in years} + 12)} \times (\textit{adult dose}) = \textit{child's appproximate dose}$$

Young's Rule should not be used with children who are in the lowest or highest size percentiles for their age group, as dosing would be less accurate. The other method of calculating pediatric doses is to use **Clark's Rule**, which relies on the weight of the child and is considered to be more accurate for medications that are affected by body size. It is calculated using the following formula:

$$\frac{(\textit{child's weight in pounds})}{(150\ \textit{pounds})} \times (\textit{adult dose}) = \textit{child's appproximate dose}$$

While weight-based dosing is the most commonly used method for calculating medication doses, no method is deemed superior to another. Clinicians use clinical judgement to determine the best method for each patient and medication.

Example 1

A pediatric patient is prescribed acetaminophen for pain. The recommended adult dose is 325 mg. The patient is 7 years old and weighs 50 lb.

a. Using Clark's Rule, calculate the dose:

$$\left(\frac{50\text{ lb}}{150\text{ lb}}\right) \times 325\text{ mg} = 108\text{ mg}$$

b. Using Young's Rule, calculate the dose:

$$\frac{7\text{ years}}{(7\text{ years} + 12\text{ years})} \times 325\text{ mg} = 120\text{ mg}$$

Recommended dosages of drugs are often expressed in the references as a number of milligrams per unit of body weight, per unit of time. For example, the recommended dose for a drug might be 6 mg/kg/24 h. This information can then be used to:

1. Calculate the dose for the individual patient
2. Check on the appropriateness of the prescribed dose, watching particularly for possible overdoses

Example 1

The recommended dose of meperidine (Demerol) is 6 mg/kg/24 h for pain, in divided doses every 4–6 h, as necessary. Demerol is available in ampules or cartridges labeled 50 mg/mL. How much Demerol would be appropriate for a 33-lb child as a single dose every 6 h?

Step 1. Convert pounds to kilograms (divide the number of pounds by 2.2):

$$\frac{33\text{ lb}}{2.2} = 15\text{ kg}$$

Step 2. Calculate the number of *mL needed in 24 h*. Write the problem as a ratio and label each term:

$$\frac{6\text{ mg}}{\text{kg}}\text{ in 24 h is recommended}$$

$$\frac{6\text{ mg}}{\text{kg}} \times 15\text{ kg} = 90\text{ mg in 24 h}$$

$$\frac{50\text{ mg}}{1\text{ mL}} = \frac{90\text{ mg}}{X\text{ mL}}$$

Step 3. Cross multiply.

$$50X = 90$$

$$\frac{50X}{50} = \frac{90}{50}$$

$$X = 1.8\text{ mL in 24 h}$$

Then calculate the number of *mL needed in 6 h*. Remember, the unknown quantity is always the last term in the equation.

$$\frac{24\text{ h}}{1.8\text{ mL}} = \frac{6\text{ h}}{X\text{ mL}}$$

$$24\text{ h }(X\text{ mL}) = 10.8$$

$$X = 0.45\text{ mL dose every 6 h}$$

Step 4. The appropriateness of this dose can be checked by applying *Clark's Rule:*

$$\frac{\text{child's wt in lb}}{\text{average adult wt}} \times \text{adult dose} = \text{child's } \textit{approximate dose}$$

$$\frac{33}{150} \times 100\text{ mg} = 22\text{ mg approximate child's dose}$$

Note: The average adult weight is 150 lb.

Demerol is available in ampules labeled $\frac{100\text{ mg}}{2\text{ mL}}$.

$$\frac{100\text{ mg}}{2\text{ mL}} = \frac{22\text{ mg}}{X\text{ mL}}$$

$$100X = 44 = 100\overline{)44.00}^{\,0.44}$$

$$X = 0.44\text{ mL dose to be administered}$$

Remember, this is a *general* rule and other variables must be considered when assessing for appropriateness of dosage.

Geriatric Dosage

Special consideration must be given to the preparation and administration of safe dosages to older adults. As with children, the dose frequently needs to be reduced. Factors leading to possible dangerous cumulative effects can include slower metabolism; poor circulation; or impairment of the liver, kidneys, lungs, or central nervous system. Any chronic disease, debility, dehydration, or electrolyte imbalance can affect assimilation of drugs and interfere with the therapeutic effect. Many drugs can impair the mental status of older adults, leading to confusion. Any older adult taking many drugs is also at risk for potentially lethal interactions. There is no formula to guide you in safe geriatric dosage. *Start low and go slow* is a good general approach to follow. Careful assessment on an *individual* basis, constant monitoring, and reduction of dosage whenever possible are the rules to follow. Each individual reacts differently to drugs, and changes occur over time. You have the responsibility to question the appropriateness of any drug, and especially as the patient's condition changes.

Prevention of Medication Errors

Medication errors can occur for a number of reasons: administering the wrong drug, in the wrong amount, at the wrong time, by the wrong route, or to the wrong patient or improperly documenting drug information. Errors can occur when the drug order is misinterpreted.

Here are rules to help avoid misinterpretation of orders:

- Never leave the decimal point naked. Writing .2 instead of 0.2 could cause the decimal point to be missed and could result in an overdose. Always place a zero *before* a decimal point, for example, 0.2, 0.5.
- Never place a decimal point and zero after a whole number. The decimal point could be missed, and the zero could be misinterpreted; for example, 5.0 mg could be read as 50 mg. The correct way is to write 5 mg.
- Avoid using decimals whenever whole numbers can be used as alternatives; for example, 0.5 g can be expressed as 500 mg.
- Have a second qualified person double-check any calculations for accuracy.
- If you have difficulty interpreting the spelling of a drug name or the number used for the dosage, or the dosage seems inappropriate, *always question* the order. Not only is this your duty, but you also have an ethical and a legal responsibility to be sure that the drugs you administer are safe. If a medication error results in legal action, you could be held accountable, even though the order was written incorrectly. You are expected to recognize inappropriate dosage, to check reference books for unfamiliar drugs, and to ask the physician or pharmacist about any questionable dosage.

Clinical Application

Use reasoning to verify and check your calculations: When doing a calculation, it is easy to make a simple math error or to use an incorrect method; this will often result in not only a wrong answer but also an unreasonable one. This is why it is important to always check your answer to determine if it is reasonable compared to the common dose and to the dosage available. For instance, if you calculate a dose that requires you to use many units of an available dose (such as 10 capsules for one dose) or a small fraction of an available dose (such as 0.01 vial), this is indicative of an incorrect calculation.

Note: When necessary, use references to obtain normal dosing ranges.

Chapter Review Quiz

Section A

Basic math review.

1. Match the following symbols with their meaning.

$+$ ___ a. multiply

$=$ ___ b. divide

$\times$ ___ c. equals

/ ___ d. addition

2. Multiply the following fractions: $\frac{22}{3} \times \frac{32}{5}$

a. $9\frac{1}{15}$

b. $\frac{54}{8}$

c. $\frac{704}{15}$

d. $\frac{10}{3}$

3. Subtract the following decimals: 10.4 – 0.037

a. 10.363

b. 10.077

c. 10.437

d. 9.363

4. Which of the following is 8% written as a reduced fraction?

a. $\frac{2}{25}$

b. $\frac{8}{100}$

c. $\frac{4}{50}$

d. $\frac{8}{1{,}000}$

Section B

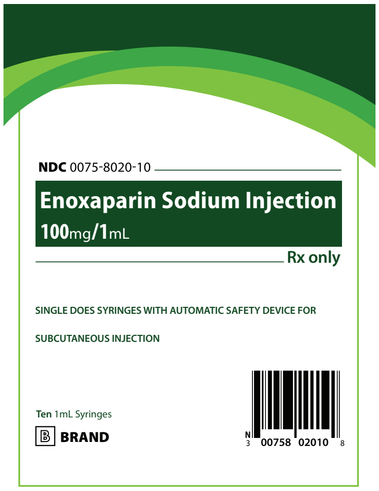
The available dosages are listed with each of the following drugs. Choose the most appropriate available form to deliver the dosage ordered. Use only *one* form of each drug. Indicate the *amount* and *which drug form* you should give for the following orders. *Use the smallest number of tablets possible. Use either the basic calculation method or the ratio and proportion method, and show your work!*

Drug and Dose Ordered	**Amount to Administer**
1. atenolol (Tenormin) 75 mg Available 50-mg and 100-mg scored tablets of Tenormin	___ of ___mg tab
2. buspirone (Buspar) 25 mg Available 5-mg and 10-mg tablets of Buspar	___ of ___mg tab
3. alprazolam (Xanax) 0.75 mg Available 0.25-mg, 0.5-mg, and 1-mg tablets of Xanax	___ of ___mg tab
4. bumetanide (Bumex) 2 mg Available 0.5-mg and 1-mg tablets of Bumex	___ of ___mg tab
5. cimetidine (Tagamet) 200 mg Available 300-mg and 400-mg tablets of Tagamet	___ of ___mg tab
6. furosemide (Lasix) 60 mg Available 20-mg, 40-mg, and 80-mg tablets of Lasix	___ of ___mg tab
7. levothyroxine (Synthroid) 0.3 mg Available 0.05-mg, 0.1-mg, and 0.15-mg tablets of Synthroid	___ of ___mg tab
8. propranolol (Inderal) 15 mg Available 10-mg, 20-mg, and 40-mg tablets of Inderal	___ of ___mg tab
9. prednisone 15 mg Available 5-mg, 10-mg, and 20-mg tablets of prednisone	___ of ___mg tab
10. sertraline (Zoloft) 75 mg Available 50-mg and 100-mg tablets of Zoloft	___ of ___mg tab

Section C

Show your work. Label and circle your answers.

1. The physician orders enoxaparin (Lovenox) $1\,\frac{\text{mg}}{\text{kg}}$ subcu q12h. The patient weighs 176 lb. Available:



NDC 0075-8020-10

Enoxaparin Sodium Injection

100mg/**1**mL

Rx only

SINGLE DOES SYRINGES WITH AUTOMATIC SAFETY DEVICE FOR SUBCUTANEOUS INJECTION

Ten 1mL Syringes

BRAND

N 3 00758 02010 8

   a. What is the patient's weight in kilograms? ___

   b. What is the dose of Lovenox to be administered? ___ mg in ___ mL.

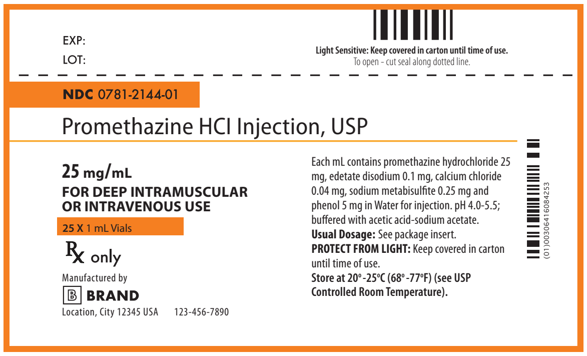
2. The medication order reads Demerol 60 mg IM. The narcotics drawer contains syringes labeled meperidine (Demerol) $\frac{75\text{ mg}}{2\text{ mL}}$.

   a. How many milliliters would you administer? ______________________________

   b. How many milliliters would you discard and mark as "wasted" on the narcotic record? ______________________________

3. Lasix is available in 40-mg tablets. The order reads Lasix 60 mg PO qAM. How many tablets should you give? ______________________________

4. Phenergan 12.5 mg IV is ordered. Available:



EXP:

LOT:

Light Sensitive: Keep covered in carton until time of use.

To open - cut seal along dotted line.

NDC 0781-2144-01

Promethazine HCI Injection, USP

25 mg/mL

FOR DEEP INTRAMUSCULAR OR INTRAVENOUS USE

25 X 1 mL Vials

℞ only

Manufactured by

BRAND

Location, City 12345 USA 123-456-7890

Each mL contains promethazine hydrochloride 25 mg, edetate disodium 0.1 mg, calcium chloride 0.04 mg, sodium metabisulfite 0.25 mg and phenol 5 mg in Water for injection. pH 4.0-5.5; buffered with acetic acid-sodium acetate.

Usual Dosage: See package insert.

PROTECT FROM LIGHT: Keep covered in carton until time of use.

Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature).

(01)00306416084253

How many milliliters would you administer? ______________________________

5. Acetaminophen elixir 650 mg PO is ordered. The container is labeled $\frac{325\text{ mg}}{5\text{ mL}}$.

a. How many milliliters would you administer? ______________________________

b. How many teaspoons per dose? ______________________________

6. Morphine sulfate PO 30-mg liquid is ordered. Morphine oral solution is labeled $\frac{20\text{ mg}}{\text{mL}}$. How many milliliters would you administer? ______________________________

7. The medication order reads heparin 5,000 units. Vials available in the medication cupboard are labeled heparin 10,000 units/mL. How many milliliters should you draw into the syringe? ______________________________

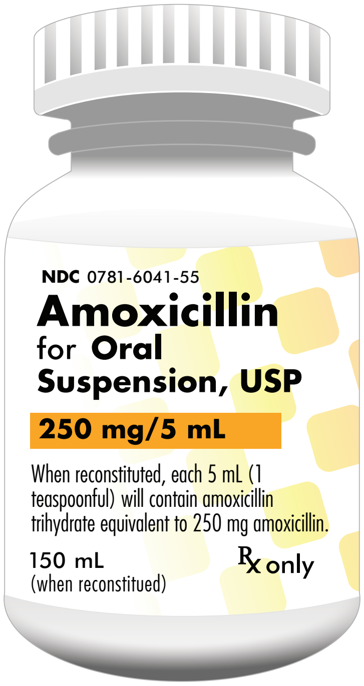
____

8. Digoxin elixir is available in 50 mcg/mL. The physician orders 125 mcg PO daily. How many milliliters should you give? ______________________________

9. The physician orders prednisone PO 7.5 mg daily. Prednisone is available in 5-mg and 10-mg scored tablets, which can be broken in half. Which strength tablet and how many tablets should you give?

____

10. Amoxicillin suspension 750 mg PO q8h is ordered. Liquid medication available:


NDC 0781-6041-55
Amoxicillin
for Oral
Suspension, USP
250 mg/5 mL
When reconstituted, each 5 mL (1 teaspoonful) will contain amoxicillin trihydrate equivalent to 250 mg amoxicillin.
150 mL
(when reconstituted)
℞ only

How many milliliters should you give? ______________________________

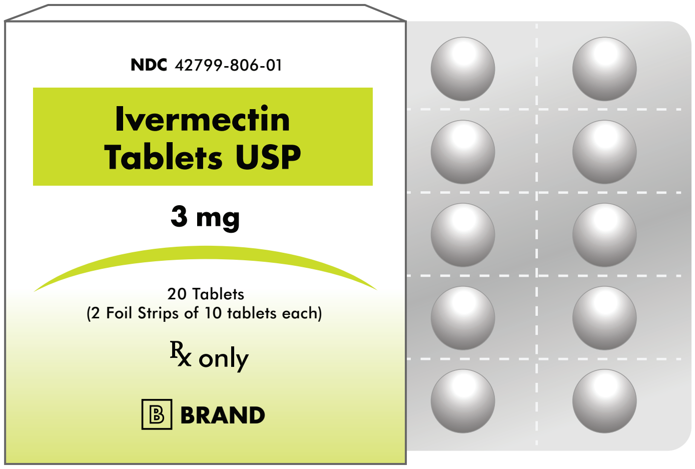
11. Calcium carbonate 1,000 mg PO daily is prescribed, to be given in divided doses bid. Available tablets contain calcium 250 mg/tab. How many tablets should be taken each time? ______________________________

____

12. Cheratussin AC contains 10 mg of codeine in each teaspoon (5 mL). If 2 tsp Cheratussin AC PO is prescribed q4h, how much codeine would be contained in each dose? ______________________________

____

13. The physician orders ivermectin tablets for a 200-lb adult with scabies. The recommended dose is 0.2 mg/kg. Available:


NDC 42799-806-01
Ivermectin Tablets USP
3 mg
20 Tablets
(2 Foil Strips of 10 tablets each)
℞ only
B BRAND

How many tablets should be given for the dose? ______________________________

14. The physician orders cefaclor (Ceclor) suspension 200 mg PO q8h for a 44-lb child. Ceclor suspension is available in $\frac{250\text{ mg}}{5\text{ mL}}$.

a. How many milliliters should be administered each time? ______________________________

b. The recommended dosage of Ceclor is 30 mg/kg/daily. How many milligrams would be appropriate for this child daily? ______________________________

15. List five variables to consider in determining a child's dose:

____________, ____________, ____________, ____________, and ____________

16. List five factors that could lead to serious cumulative effects with medicines in older adults:

____________, ____________, ____________, ____________, and ____________

Chapter 7

Responsibilities and Principles of Drug Administration

Key Terms and Concepts

Confirmation bias

Documentation of drug administration

Medication Errors Reporting (MER) program

Medication reconciliation

MedWatch

Reporting of medication errors

Responsibilities of drug administration

Sentinel events

Seven Rights of Medication Administration

Objectives

Upon completion of this chapter, the learner should be able to:

1. List at least four responsibilities of the health care professional in safe administration of medications.
2. List the seven Rights of Medication Administration.
3. Explain moral, ethical, and legal responsibilities regarding medication errors.
4. Describe two instances of medication administration that require documentation.
5. Explain the rights of the health care professional to question or refuse to administer medications.

Responsible Drug Administration

The safe and accurate administration of medications requires knowledge, judgment, and skill. The **responsibilities of drug administration** of the health care professional in this vital area are as follows:

1. Adequate, up-to-date *information* about all medications to be administered, including their purpose, potential side effects, cautions and contraindications, and possible interactions

2. *Wisdom* and judgment to accurately *assess* the patient's needs for medications, to *evaluate* the response to medications, and to *plan* appropriate interventions as indicated
3. *Skill in delivery* of the medication accurately, in the best interests of the patient, and with adequate documentation
4. *Patient education* to provide the necessary information to the patient and family about why, how, and when medications are to be administered and their potential side effects and precautions with administration by the layperson

Responsibility for safe administration of medications requires that the health care professional be familiar with every medication before administration. Knowledge of the typical and most frequently used drugs to treat the body systems is imperative. However, this is only a framework upon which to build and add other knowledge of new drugs or new effects as changes in medicine become known. Unfamiliar drugs should never be administered. Resources such as the *PDR*, the *AHFS Drug Information*, the *USP/DI*, package inserts, linked electronic resources such as Micromedex, or pharmacists must be consulted *before* administering a drug to become familiar with its desired effect, potential side effects, cautions and contraindications, and possible interactions with other drugs or with foods.

Responsibility for safe administration of medications requires *complete planning* for patient care, including prior *assessment*, *interventions*, and *evaluations* of the results of drug therapy. Assessment involves taking a complete history, including all medical conditions (e.g., pregnancy or illness), allergies, and all other medications in use, including over-the-counter drugs, vitamins, and herbal remedies. Assessment also involves careful observation of the patient's vital signs, posture, skin temperature and color, and facial expression before and after drug administration. Appropriate interventions require judgment in timing, discontinuing medicine if required, and taking steps to counteract adverse reactions, as well as knowing what and when to report to the physician. Evaluation and documentation of results also play a vital role for all health care professionals, including the physician, in planning effective drug therapy.

The safe administration of medications necessitates training to develop skills in the delivery of medications. The goal is to maximize the effectiveness of the drug with the least discomfort to the patient. Sensitivity to the unique needs of each patient is encouraged (e.g., awareness of difficulty swallowing or impaired movement that could affect medication administration).

Patient education is an essential part of the safe administration of medicines. If patients are to benefit from drug therapy, they must understand the importance of taking the medicine in the proper dosage, at the proper (correct) time, and in the proper way. Information for patients should be in the language they understand and should include both verbal and written instructions as well as demonstrations of techniques when indicated. If the medication administration requires extra equipment or has multiple steps, a return demonstration should be required.

Administration of medication carries moral, ethical, and legal responsibilities. Some rules and regulations vary with the institution, agency, or office. When in doubt, consult those in authority—supervisors or administrators—and/or policy and procedure books. However, documentation in the patient's record is always required for all medicines given as well as for patient education. In addition, controlled substances given must also be recorded in a narcotics record.

Medication Errors

Medication errors can and do occur in all health care settings. More errors are reported from acute care settings, where the risk is greatest. However, professionals in outpatient facilities, ambulatory care sites, home health care, and long-term care facilities have challenges unique to their practices as well. Patients in these settings often are older adults and are likely to have several chronic conditions requiring multiple medications. Increasing the number of medications an individual receives not only increases the risk of interactions and adverse side effects, but also increases the risk of error.

Medication errors can occur in the following situations:

1. Administering a drug to the *wrong* patient
2. Administering the *wrong* drug or drug form
3. Administering a drug via the *wrong* route
4. Administering a drug using the *wrong* technique
5. Administering a drug at the *wrong* time
6. Administering the *wrong* dosage
7. *Wrong* documentation: improperly documenting drug administration information on a patient's medical record

Meticulous care in preparation and administration of medications reduces the chances of error. However, if a mistake is made, it is of the utmost importance to *report it immediately* to the person in charge so that corrective action can be taken for the patient's welfare. For justification in case of legal proceedings, the patient's record should reflect the corrective action taken. An incident report must also be completed as a legal requirement. Failure to report errors appropriately can jeopardize the patient's welfare, as well as increase the possibility of civil suits against the health care professional and/or the risk of loss of professional license or certificate. Honesty is not only the best policy, but it is also the *only* policy for moral, ethical, and legal reasons.

Sentinel events are patient safety events that result in death, permanent harm, or severe temporary harm. Medication errors are often sentinel events. It is important that you complete the required incident report, which goes to the risk management department and then is routed to the appropriate accrediting body. The goal of this reporting is to prevent future incidents. New policies and procedures are often created based off root cause analysis of incident reports.

Health care professionals have a responsibility to provide quality care and provide for patient safety at all times. Remember, *First, do no harm*. This challenge includes prevention of medication errors and also **reporting of medication errors** so that corrective steps can be taken.

The Agency for Healthcare Research and Quality has federally certified the Institute for Safe Medication Practices (ISMP) as a Patient Safety Organization (PSO) to operate a national error-reporting program for both vaccine and medication errors. Health care professionals and the public should be encouraged to report errors to ISMP because a PSO confers both privilege and confidentiality to the information reported. Error reporting by health care professionals and hospitals is necessary to develop safety alerts and quality improvement programs. As part of this goal, the *U.S. Pharmacopeia (USP)* has established a **Medication Errors Reporting (MER) program**, which can be accessed online at www.ismp.org/report-medication-error.

Medication reconciliation is a method used to compare the medications a patient is taking to the medications ordered by the patient's physician. This comparison is done every time there is a change in the patient's care. For example, medication reconciliation is done whenever a patient is admitted, transferred, or discharged from the hospital. It is performed at follow-up physician visits to ensure accuracy and compliance. Medication reconciliation is done to prevent medication errors caused by omissions, duplications, errors in doses, or medication interactions.

According to the Joint Commission, medication reconciliation consists of five steps:

1. Develop a list of current medications.
2. Develop a list of medications to be prescribed.
3. Compare the medications on the two lists.
4. Make clinical decisions based on the comparison.
5. Communicate the new list to appropriate caregivers and to the patient.

Principles of Administration

When preparing to administer medications, several basic principles should always be kept in mind:

1. *Cleanliness:* Always wash hands before handling medicines, and be sure the preparation area is clean and neat. Wear any required personal protective equipment (PPE).
2. *Organization:* Always be sure medications and supplies are in the appropriate area and in adequate supply. When stock drugs are used, they should be reordered immediately.
3. *Preparation area:* Ensure this area is well lighted and away from distracting influences.

Guidelines to review before administering medicines are called the **Seven Rights of Medication Administration** (Figure 7-1):

1. Right medication and dosage form
2. Right amount
3. Right time

4. Right route
5. Right patient
6. Right documentation
7. Right technique

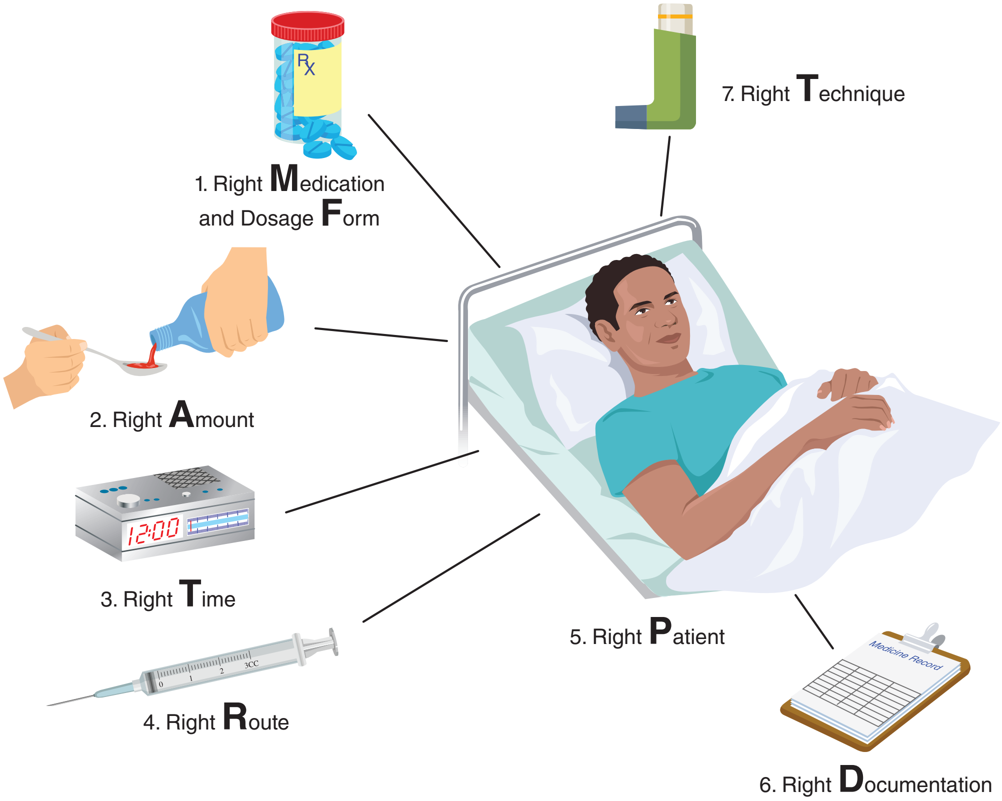


Figure 7-1 The Seven Rights of Medication Administration.

Right Medication and Dosage Form

Please note that many health care facilities develop medication policies that list many more "rights" and/or steps. Always follow the guidelines of your particular facility. You can confirm that you have the right medication by carefully comparing the name of the drug prescribed (on the physician's order sheet, prescription blank, medication record, or medicine card) with the label on the package, bottle, or unit dose packet (medications with each dose separately sealed in an individual paper, foil, plastic, or glass container). *Never* give medication when the name of the medication is obscured in any way. Some drugs have names that sound or look similar (e.g., Novolin 70/30 and Novolog Mix 70/30), and therefore it is essential to scrutinize every letter in the name when comparing the medicine ordered with the medicine on hand. Accuracy can be facilitated by placing the unit-dose packet next to the name of the drug ordered on the patient's record, while comparing the drug ordered with the drug on hand.

Always confirm that you have the correct dosage form. The most common mistake made regarding dosage forms is substituting a capsule for a tablet or vice versa, but you should always double-check the dosage form for all medications. Choosing the incorrect dosage form may not seem like a major issue, but it can cause vastly different pharmacological effects for the patient. Whereas tablets are often intended to dissolve in the acidic stomach, some capsules are specifically designed to not dissolve until they reach the more basic small intestine. Selecting the wrong dosage form could lead to decreased efficacy of the drug. Some medications that have both a capsule and tablet form are actually used completely differently in practice. For example, hydroxyzine in tablet form is generic for the brand name Atarax, but in capsule form is generic for the brand name Vistaril. Whereas Atarax is primarily used for acute puritis (itching), Vistaril is often used as an adjunct therapy for depression and anxiety. Additionally, medications that come in both a capsule and a tablet are much different in cost, meaning selecting the correct dosage form is important to the financial costs to the patient.

If there is any question about the drug order because of handwriting, misspelling, inappropriateness, allergies, or interactions, you have the *right and responsibility to question* the physician and/or the pharmacist.

Never give medications that someone else has prepared. *Never* leave medications at the bedside unless this is specifically ordered by the physician (e.g., nitroglycerin tablets and contraceptives are frequently ordered to be left with the patient for self-administration). If the patient is unable to take a medication when you present it, the medication must be returned (in an unopened packet) to the patient's drawer in the medicine cart or medicine room. Never open the unit-dose packet until the patient is prepared to take the medicine.

Right Amount

Administering the right amount of drug is extremely important. The drug dosage ordered must be compared *very carefully* with the dose listed on the label of the package, bottle, or unit-dose packet. Here again, accuracy can be facilitated by placing the unit-dose packet next to the written order on the patient's record while comparing the dose ordered with the dose on hand.

The different systems of measurement include household, apothecary, and metric. It is important to consult a table of equivalents if necessary to convert from one system to another. Drug calculations are infrequent with unit-dose packaging. However, if it is necessary to compute calculations, such calculations must be checked by another trained health care professional, pharmacist, or physician to verify accuracy. Be especially careful when the dose is expressed in decimals or fractions. Always recheck the dose if less than ½ tablet or more than 2 tablets, or if more than 2 mL for injection is required. An unusual dosage should alert you to the possibility of error. Those who administer medications have the right, as well as the responsibility, to question any dosage that is unusual or seems inappropriate for the individual patient. Remember that drug action is influenced by the patient's condition, metabolism, age, weight, sex, and psychological state. The health care professional has the responsibility of reporting the results of careful assessment and observations to assist the physician in prescribing the right dosage for each patient.

An important part of patient education includes complete instructions about the importance of preparing and taking the right amount of medicine prescribed by the physician.

Right Time

The time for administration of medications is an important part of the drug *dosage*, which includes the amount, frequency, and number of doses of medication to be administered. For maximum effectiveness, drugs must be given on a prescribed schedule. The physician's order specifies the number of times per day the medicine is to be administered (e.g., bid or twice a day). Some medications need to be maintained at a specific level in the blood (*therapeutic level*) and are therefore prescribed at regular intervals around the clock (e.g., q4h or every four hours). Some medications, such as some antibiotics, are more effective on an empty stomach and are therefore prescribed *ac* (before meals). Medications that are irritating to the stomach are ordered *pc* (after meals). Drugs that cause sedation are more frequently prescribed at hour of sleep. If the physician does not prescribe a specific time for administration of a drug, the health care professional arranges an appropriate schedule, taking into consideration the purpose, action, and side effects of the medication. Patient education includes instruction about the right time to take specific medicines and why.

Right Route

The route of administration is important because of its effect on degree of absorption, speed of drug action, and side effects. Many drugs can be administered in a variety of ways. The physician's order specifies the route of administration. Those administering medications have the right and responsibility to question the appropriateness of a route based on assessment and observation of the patient. Change of route may be indicated because of the patient's condition (e.g., nausea, vomiting, or difficulty swallowing). However, the route of administration may not be changed without the physician's order.

Right Patient

The patient who is to receive the medication must be identified by the use of certain techniques to reduce the chance of error. In health care facilities, the patient's wrist identification band should be checked *first*, and then the patient should be called by name or asked to state their name *before* the medication is administered. In the ambulatory care setting, the patient can be asked to give their name and date of birth; this can be verified with the chart before administering medications. If the patient questions the medication or the dosage, recheck the order and the medicine before giving it.

Right Documentation

Another essential duty is **documentation of drug administration**. Every medication given must be recorded on the patient's record, along with *dose*, *time*, *route*, and *location* of injections. In addition, any unusual or adverse patient reactions must be noted. If the medication is given on a PRN (as necessary) basis (e.g., for pain), notation should also be made on the patient's record regarding the effectiveness of the medication. The person administering the medication must also sign or initial the record after administration (the policy of each facility determines the exact procedure to be followed). The accuracy of medication documentation is a very important legal responsibility. At times, patients' records are examined in court, and the accuracy of medication documentation can be a critical factor in some legal judgments.

Documentation also includes the recording of narcotics administered on the special controlled substances record kept with the narcotics. If narcotics are destroyed because of partial dosage, cancellation, or error, two health care professionals must sign as witnesses of the disposal of the drug (the policy about documentation of narcotics may vary by agency).

Right Technique

Part of the medication order is the route. Each route and each medication may have specific rules that apply regarding the technique for administering. The prescriber will not specify this technique; this is information that the person administering the medication must know. For example, enoxaparin (Lovenox) is administered subcutaneously as an anticoagulant. It comes in a prefilled syringe with an air bubble. It should be given only in the abdomen, and the air bubble should not be removed prior to administration. These instructions can be found in the literature found in the package insert.

In summary, safe and effective administration of medications involves current drug information; technical and evaluation skills; and moral, ethical, and legal responsibilities. Guidelines include the Seven Rights of Medication Administration. In addition, the health care professional has the right and responsibility to question any medication order that is confusing or illegible or that seems inappropriate, as well as the right to refuse to administer any medication that is not in the best interests of the patient. The welfare of the patient is the primary concern in the administration of medications.

MedWatch

The Food and Drug Administration (FDA) issued a form in 1993 to assist health care professionals in reporting serious adverse events or product quality problems associated with medications, medical devices, or nutritional products regulated by the FDA—for example, dietary supplements and infant formulas. Even the large, well-designed clinical trials that precede FDA approval cannot uncover every problem that can come to light once a product is widely used. For example, a drug could interact with other drugs in ways that were not revealed during clinical trials. Reports by health care professionals can help ensure the safety of drugs and other products regulated by the FDA.

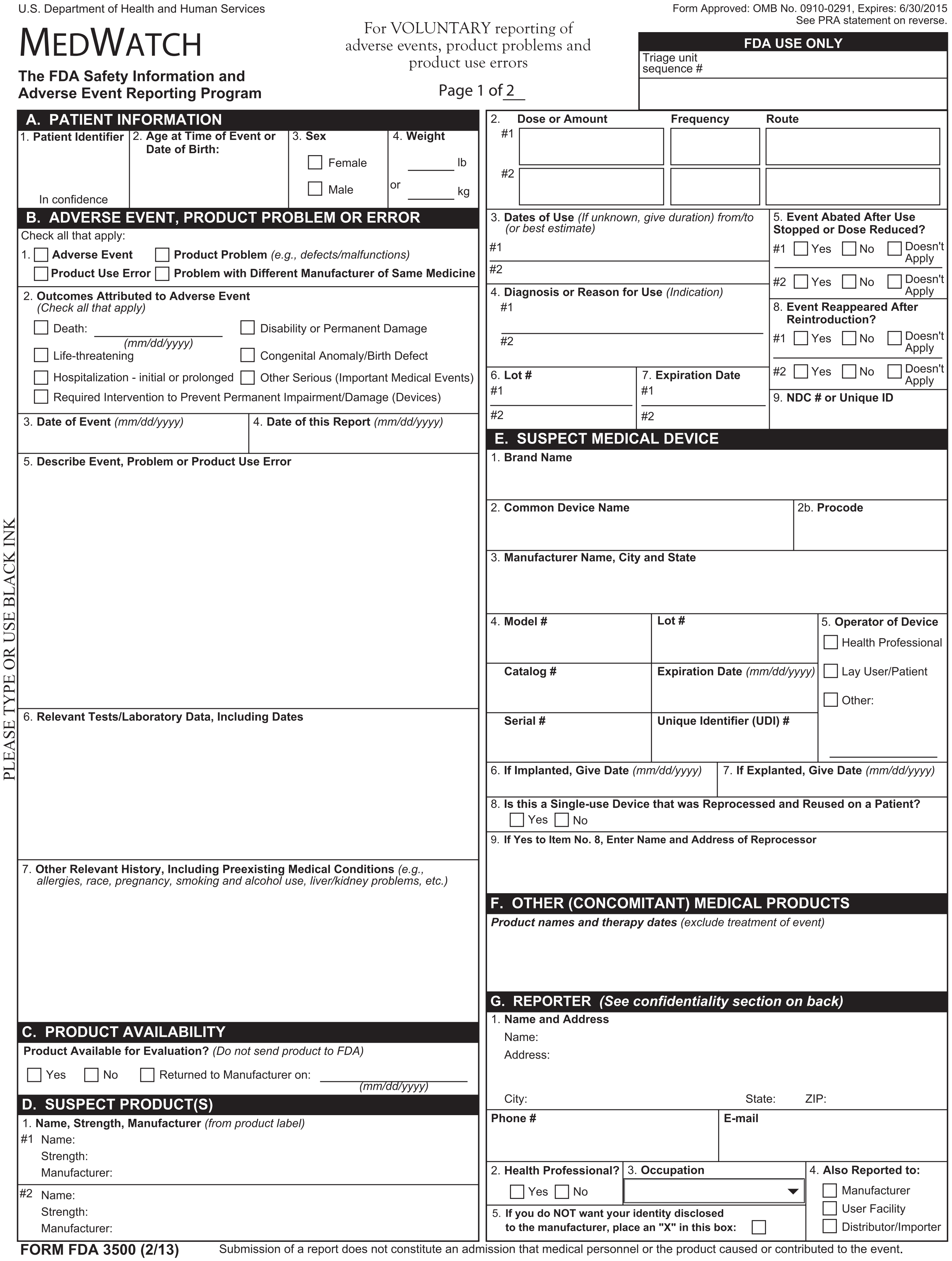
In response to these voluntary reports from the health care community, the FDA has issued warnings, made labeling changes, required manufacturers to do postmarketing studies, and ordered the withdrawal of certain products from the market. Such actions can prevent injuries, suffering, disabilities, congenital deformities, and even deaths.

You are not expected to establish a connection or even wait until the evidence seems overwhelming. The agency's regulations will protect your identity and the identities of your patient and your facility. With your cooperation, **MedWatch** can help the FDA to monitor product safety and, when necessary, take swift action to protect you and your patients. MedWatch encourages you to regard voluntary reporting as part of your professional responsibility. Refer to Figure 7-2 for a partial MedWatch form and for instructions on completing and submitting this form to the FDA. In addition, you can complete a MedWatch online voluntary reporting form (3500) by visiting https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program.

Clinical Application

Confirmation Bias

As a health care professional, each day you might be responsible for reviewing many medication orders for correctness before administering them to a patient. Often when a person is in a routine, they will read a medication order and notice what they expect to notice. For example, an order reads: metformin 1,000 mg tid. Metformin is almost always given twice daily, so it would be easy for a person to expect to notice "BID" and read it as such. This type of mistake most often results from noticing the same thing multiple times and is more common when a person is hurried or stressed. This phenomenon is known as **confirmation bias**. Confirmation bias accounts for many medication-related errors, but it can be easily avoided if you are diligent in checking the seven rights.



U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page 1 of 2

Form Approved: OMB No. 0910-0291, Expires: 6/30/2015
See PRA statement on reverse.

FDA USE ONLY

Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. **Patient Identifier** In confidence	2. **Age at Time of Event or Date of Birth:**	3. **Sex** ☐ Female ☐ Male	4. **Weight** _______ lb or _______ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ **Adverse Event** ☐ **Product Problem** *(e.g., defects/malfunctions)*
☐ **Product Use Error** ☐ **Problem with Different Manufacturer of Same Medicine**

2. **Outcomes Attributed to Adverse Event** *(Check all that apply)*
☐ Death: ______________ *(mm/dd/yyyy)*
☐ Disability or Permanent Damage
☐ Life-threatening
☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - initial or prolonged
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. **Date of Event** *(mm/dd/yyyy)*
4. **Date of this Report** *(mm/dd/yyyy)*

5. **Describe Event, Problem or Product Use Error**

6. **Relevant Tests/Laboratory Data, Including Dates**

7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*

☐ Yes ☐ No ☐ Returned to Manufacturer on: ______________ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. **Name, Strength, Manufacturer** *(from product label)*
#1 Name:
Strength:
Manufacturer:
#2 Name:
Strength:
Manufacturer:

	Dose or Amount	**Frequency**	**Route**
2. #1			
#2			

3. **Dates of Use** *(If unknown, give duration) from/to (or best estimate)*
#1
#2

5. **Event Abated After Use Stopped or Dose Reduced?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

4. **Diagnosis or Reason for Use** *(Indication)*
#1
#2

8. **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. **Lot #**
#1
#2

7. **Expiration Date**
#1
#2

9. **NDC # or Unique ID**

E. SUSPECT MEDICAL DEVICE

1. **Brand Name**

2. **Common Device Name**
2b. **Procode**

3. **Manufacturer Name, City and State**

4. **Model #**
Lot #
Catalog #
Expiration Date *(mm/dd/yyyy)*
Serial #
Unique Identifier (UDI) #

5. **Operator of Device**
☐ Health Professional
☐ Lay User/Patient
☐ Other:

6. **If Implanted, Give Date** *(mm/dd/yyyy)*
7. **If Explanted, Give Date** *(mm/dd/yyyy)*

8. **Is this a Single-use Device that was Reprocessed and Reused on a Patient?**
☐ Yes ☐ No

9. **If Yes to Item No. 8, Enter Name and Address of Reprocessor**

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*

G. REPORTER ***(See confidentiality section on back)***

1. **Name and Address**
Name:
Address:
City: State: ZIP:

Phone #
E-mail

2. **Health Professional?**
☐ Yes ☐ No

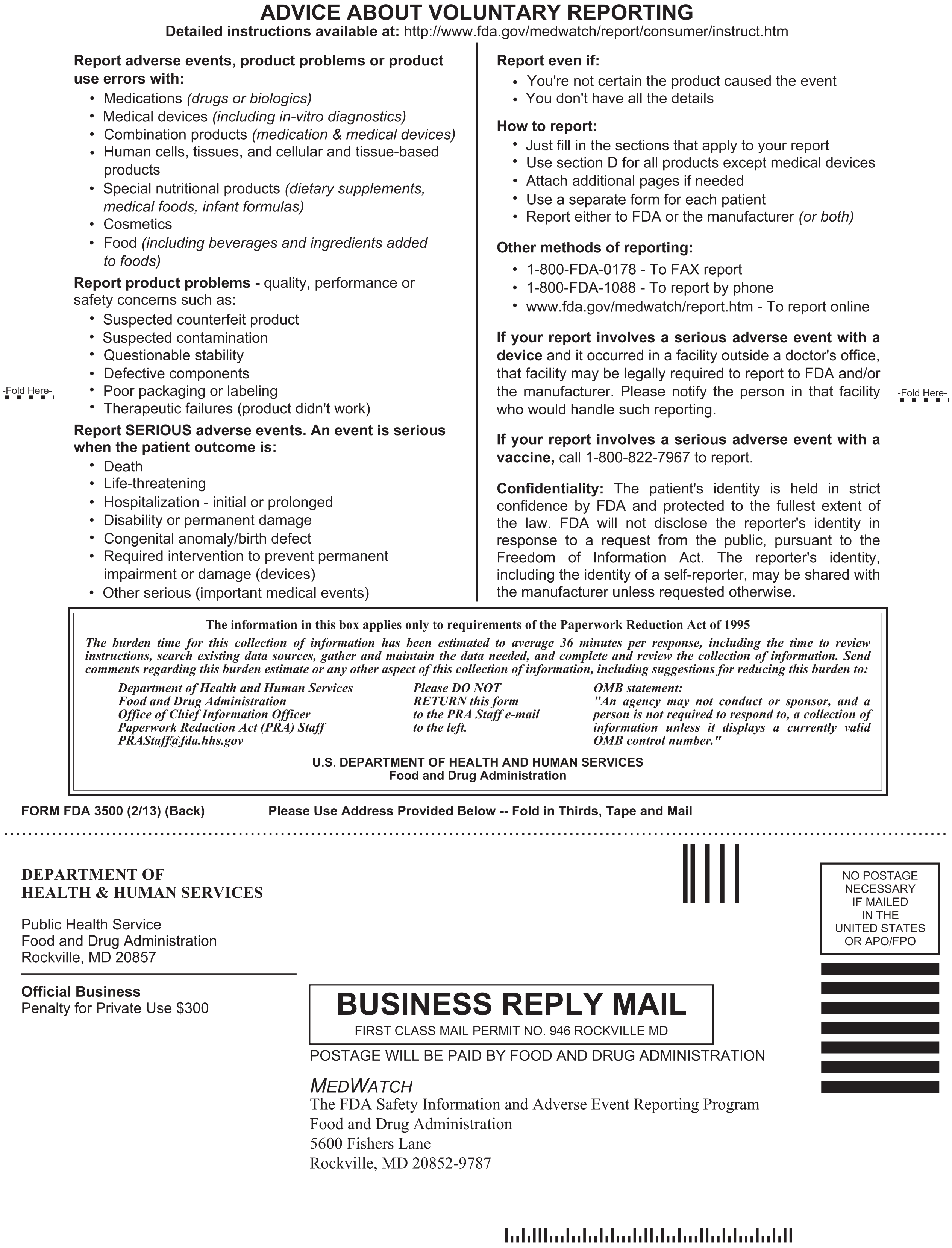
3. **Occupation**

4. **Also Reported to:**
☐ Manufacturer
☐ User Facility
☐ Distributor/Importer

5. **If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box:** ☐

FORM FDA 3500 (2/13) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Figure 7-2 MedWatch form. The FDA Medical Products Reporting Program for voluntary reporting by health professionals of adverse events and product problems. Visit https://www.fda.gov for the complete, interactive MedWatch form, and instructions for completing.



ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: http://www.fda.gov/medwatch/report/consumer/instruct.htm

Report adverse events, product problems or product use errors with:

- Medications *(drugs or biologics)*
- Medical devices *(including in-vitro diagnostics)*
- Combination products *(medication & medical devices)*
- Human cells, tissues, and cellular and tissue-based products
- Special nutritional products *(dietary supplements, medical foods, infant formulas)*
- Cosmetics
- Food *(including beverages and ingredients added to foods)*

Report product problems - quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

-Fold Here-

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization - initial or prolonged
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage (devices)
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details

How to report:

- Just fill in the sections that apply to your report
- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer *(or both)*

Other methods of reporting:

- 1-800-FDA-0178 - To FAX report
- 1-800-FDA-1088 - To report by phone
- www.fda.gov/medwatch/report.htm - To report online

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

-Fold Here-

If your report involves a serious adverse event with a vaccine, call 1-800-822-7967 to report.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

The information in this box applies only to requirements of the Paperwork Reduction Act of 1995

The burden time for this collection of information has been estimated to average 36 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed, and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

Please DO NOT RETURN this form to the PRA Staff e-mail to the left.

OMB statement:
"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FORM FDA 3500 (2/13) (Back) **Please Use Address Provided Below -- Fold in Thirds, Tape and Mail**

DEPARTMENT OF
HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Official Business
Penalty for Private Use $300

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES
OR APO/FPO

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 946 ROCKVILLE MD

POSTAGE WILL BE PAID BY FOOD AND DRUG ADMINISTRATION

MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Figure 7-2 Continued

Chapter Review Quiz

Complete the statements by filling in the blanks.

1. According to the Joint Commission, medication reconciliation consists of what five steps?

2. Before administering any medication, you should have the following three pieces of information about the patient:

3. When preparing to administer medications, what three principles should be kept in mind?

4. Patient education about medication should include the following four pieces of information:

5. When administering a controlled substance, documentation is necessary in what two places?

6. Documentation of an injection given for pain should include the following five pieces of information:

7. Name the Seven Rights of Medication Administration:

8. Medication errors must be reported immediately, and documentation includes recording the information in the following two areas:

9. Discuss a situation in which the health care professional would refuse to administer a medication.

10. The health care professional was reading the order and due to the poor handwriting they were unsure of the spelling of the drug to administer. The health care professional should:

a. not give the drug

b. give the drug and watch for side effects

c. question the physician

d. change the drug to what they think it should be

11. A patient asked to leave their medication at the bedside in the hospital. What should be done?

a. tell them that is never allowed

b. leave it if they trust the patient

c. leave it if it is ordered by the physician

d. leave it with instructions to take only when needed

Chapter 8

Administration by the Gastrointestinal Route

Key Terms and Concepts

Aspiration
Dysphagia
Meniscus
Nasogastric tube (NGT) medication administration
Oral medication administration
Percutaneous endoscopic gastrostomy (PEG) tube
Percutaneous endoscopic gastrostomy (PEG) tube medication administration
Rectal medication
Rectal route
Retention enema

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe the advantages and disadvantages of administering medications orally, rectally, or by percutaneous endoscopic gastrostomy (PEG) or nasogastric tube (NGT).
2. Explain the appropriate action to be taken when a patient is NPO (ordered to have nothing by mouth), has dysphagia, refuses medication, vomits medication, or has allergies.
3. List the special precautions to be followed in the preparation of sustained-release capsules, enteric-coated tablets, and oral suspensions.
4. Demonstrate the measurement of liquid medications using a medicine cup and syringe.
5. Demonstrate proficiency in administering oral medications.
6. Demonstrate proficiency in administering rectal medications.
7. Describe administration by percutaneous endoscopic gastrostomy (PEG) and nasogastric tube (NGT).

Medications are administered by the gastrointestinal route more often than any other way. Gastrointestinal administration includes four categories: oral, rectal, percutaneous gastrostomy (PEG) tube, or nasogastric tube (NGT). We will cover all these routes for your familiarity; however, the main focus will be on oral and rectal administration.

Advantages of the **oral medication administration** include the following:

- Convenience and patient comfort
- Safety because some medication can be retrieved in case of error or intentional overdose
- Economy because there are few equipment costs and most medications are formulated for this route

Disadvantages of the oral route include:

- Slower onset of absorption and action
- Rate and degree of absorption vary with gastrointestinal contents and motility
- Some drugs (e.g., insulin and heparin) are destroyed by digestive fluids and must be administered by injection
- Difficult to use in patients with nausea or vomiting
- Because of possible **aspiration**, dangerous to use if patient has difficulty swallowing (**dysphagia**). **Aspiration** is the inhalation of a foreign substance or regurgitated gastric contents, which can cause severe lung damage.
- Cannot be used for unconscious patients
- May not be able to be used if patient is NPO (e.g., before surgery, because of an acute medical condition, or if a patient is fasting for a test such as a lipid panel or scan). Normally maintenance medications can still be taken with clear liquids.
- Administration of medications by nasogastric tube, small-bore silicone gastric tube, or **percutaneous endoscopic gastrostomy (PEG) tube** is sometimes ordered when the patient is unable to swallow for periods of time because of illness, trauma, surgery, or unconsciousness. Medications are usually administered intravenously when these conditions exist for short periods of time. Each provider should be aware of which routes of administration are in their specific scope of practice.

Advantages of the PEG and NGT include:

- Ability to bypass the mouth and pharynx when necessary
- Elimination of numerous injections

Disadvantages of the PEG and NGT with a conscious patient include:

- The discomfort of the tube in the nose and throat for prolonged periods of time

Medications are sometimes administered by the **rectal route** when nausea or vomiting is present, or the patient is unconscious or unable to swallow.

Advantages of the rectal route include:

- Bypassing the action of digestive enzymes
- Avoidance of irritation to the upper GI tract
- Usefulness with dysphagia

Disadvantages of the rectal route include:

- Many medications are unavailable in suppository form
- Some patients have difficulty retaining suppositories (e.g., older adults and children)
- Prolonged use of some rectal suppositories (e.g., bisacodyl) can cause rectal irritation
- Absorption may be irregular or incomplete if feces are present

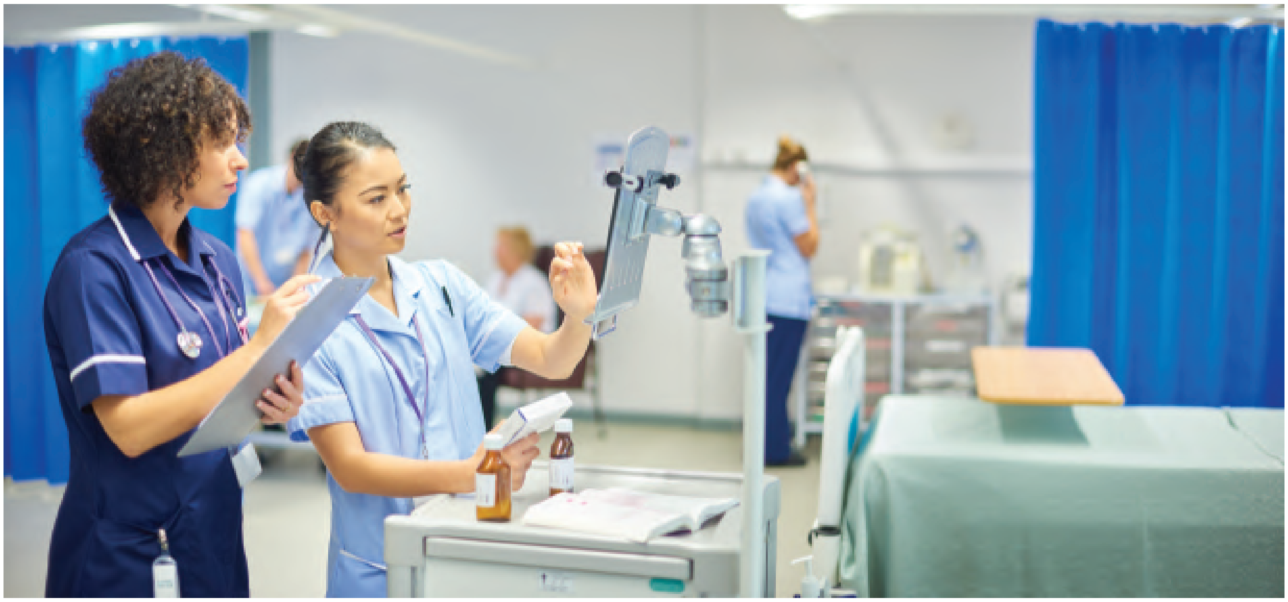
Administration of Medications Orally

Guidelines for Administration of Oral Medications

1. Wash your hands (Figure 8-1).
2. Locate the appropriate medication order or medication sheet; or, if using an eMAR, scan the patient's wristband and check for completeness of the order (i.e., date, patient's name, medication name, dosage, route, and time).
3. Check for special circumstances (e.g., allergies or NPO).
4. Be sure that you know the purpose of the drug, possible side effects, contraindications, precautions, interactions, and normal dosage range. If unfamiliar with the drug, consult a reference source for this information.
5. Select the appropriate receptacle in which to place the medication (i.e., paper medicine cup for tablets or capsules and plastic medicine cup for liquids).
6. Locate medication in the medication cupboard or medication cart drawer. If using an eMAR, scan it and compare the label screen; if using a paper record, compare the medication to the chart for the Seven Rights of Medication Administration: right medicine, right amount, right time, right route, right patient, right technique, and right documentation (Figure 8-2). Also be sure to check the drug's expiration date.
7. If the dose ordered differs from the dose on hand, complete calculations on paper and check for accuracy with your instructor or a co-worker in the clinical setting.

Offset/Shutterstock.com

Figure 8-1 Medical asepsis handwash.



iStock.com/sturti.

Figure 8-2 Compare the name and dosage on the medication package with the medication administration record.

8. Prepare the dosage as ordered. Do not open unit-dose packages until you are with the patient (Figure 8-3). If medication is liquid, refer to "Preparation of Liquid Medications" later in this section.
9. Take medication in a cup to the patient and place it on a table nearby.
10. Check the patient's identification bracelet (Figure 8-4). Ask the patient to *tell you* their name and date of birth (DOB). Compare this information with the medication administration record to verify that you have the right patient. If the patient is unable to provide their name and/or DOB, use an alternate method to identify the patient such as a photograph or identity confirmation by a family member, friend, or co-worker.

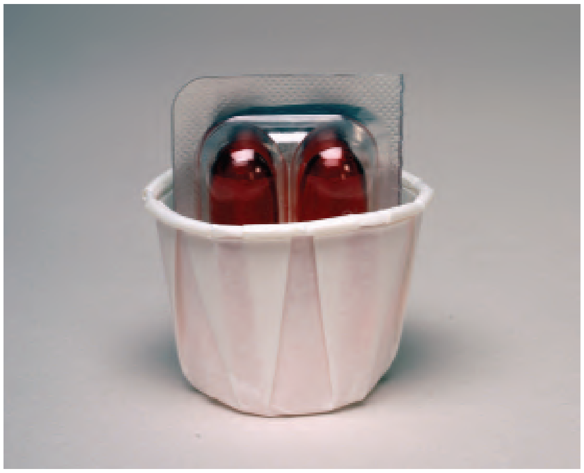


Figure 8-3 Keep the unit-dose packet intact until you are with the patient.

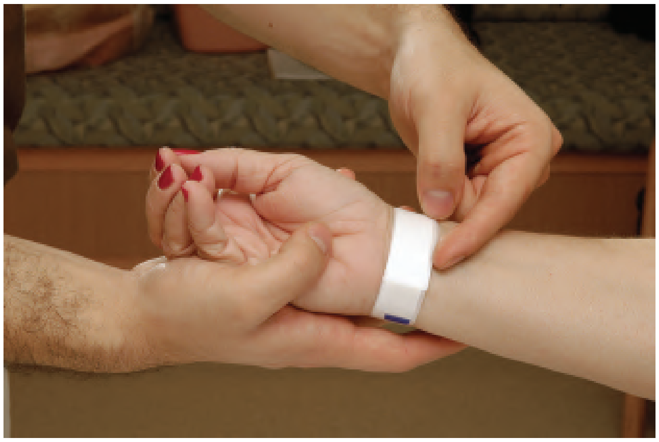


Figure 8-4 Check identification to be sure it is the right patient. Also ask the patient for their name and date of birth and verify with the medication record. Always check for allergies.

11. Call the patient by name and explain what you are doing. Answer any questions. Recheck the medication order if the patient expresses any doubts. Use this opportunity for patient education about the medication.
12. Monitor the patient's vital signs if required for the specific medication (e.g., blood pressure, apical pulse, or respiration). Blood pressure should always be taken and recorded *before* administering antihypertensives.
13. Open the unit-dose package and place the container in the patient's hand. Avoid touching the medication (Figure 8-5).
14. Provide a full glass of water and assist the patient as necessary (e.g., raise the head of the bed and provide a drinking straw if required).
15. Stay with the patient until the medication has been swallowed. Make the patient comfortable before you leave the room.
16. Discard the used medicine cup and wrappers in a wastebasket.
17. Record the medication, dosage, time, route, and your signature or initials in the correct place on the patient's record according to the rules of the facility. *Note:* in many facilities, the LOT number and expiration date of drugs dispensed or administered is recorded electronically for future reference.
18. Document on the patient's record and report if a medication is withheld or refused and the reason. Record and *report* any unusual circumstances associated with administration or any adverse side effects.

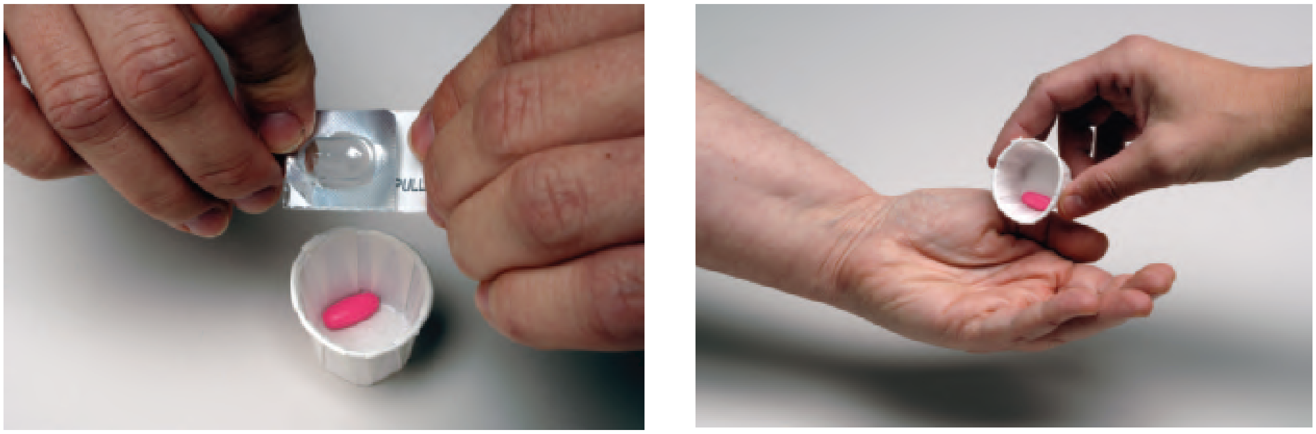


Figure 8-5 Do not touch medicine. (A) Open the unit-dose packet and drop the tablet in a cup. (B) Place the medicine in the patient's hand.

Special Considerations for Oral Administration

1. If the patient is NPO, check with the person in charge regarding the appropriate procedure, based on the reason for NPO. If the patient is fasting for tests, medication can usually be given at a later time with possible modification of time schedule or with clear liquids if the physician approves. If the patient is NPO for surgery, nausea, or dysphagia, it may be necessary to consult the doctor regarding a change of route. Do not omit the medications completely without specific instructions to that effect. Abrupt withdrawal of some medications, for example, phenytoin (Dilantin) or diazepam (Valium), may lead to dangerous conditions, such as seizures.

2. *Always check the patient's record carefully for allergies* and be aware of the components of combination products. Patients with a history of allergies should be watched carefully for possible drug reactions when any new medication is administered.
3. Give the most important medicine first; for example, cardiac medicine before a vitamin.
4. Elevate the patient's head, if not contraindicated by the patient's condition, to aid in swallowing.
5. Stay with the patient until the medication is swallowed. *Do not* leave the medication at the bedside or in the patient's possession unless this is ordered by the physician.
6. Administer oral medications with water unless ordered otherwise. *Do not* give medicine with fruit juice, milk, or any other liquid unless indicated by specific directions. The absorption of many medicines (e.g., antibiotics) is inhibited by interaction with acidic or alkaline products.
7. Medications whose action depends on contact with the mucous membranes of the mouth or throat (e.g., topical anesthetics or fungicides) *should not* be administered with any fluid or food.
8. If tablets must be divided, *do not* break by hand. If available, a pill-cutter may be used. In home care settings, cut with a knife on score marks only.
9. When removing tablets or capsules from a stock bottle, pour them into the lid and from there into the medicine cup. *Do not* touch tablets or capsules.
10. *Do not* administer any medication that is discolored, has precipitated, is contaminated, or is outdated.
11. If a patient is NPO, refuses the medication, or vomits within 20–30 min of taking the medication, always report this to the person in charge. An order from the physician is required to change either the medication or the route of administration. Document on the patient's record the time of emesis and appearance of the emesis to check whether the medication remained intact.
12. If the patient refuses a medication, determine the reason. Report the refusal and reason to the person in charge and record all information on the patient's record.
13. Tablets (unless enteric coated or sustained-release) may be crushed with mortar and pestle or pill-crusher. Some capsules (even sustained-release capsules) may be opened and the contents mixed with applesauce, pudding, or ice cream to facilitate administration for patients with difficulty swallowing (e.g., children and older adults). Do not crush the contents of a sustained-release capsule or allow patients to chew it. If a patient is unable to swallow a tablet or capsule whole, the package insert should be reviewed or a pharmacist should be consulted to make sure it is allowable to disrupt the original dosage form. Check the patient's diet to be sure these foods are allowed. Be sure that any equipment used to crush medication is wiped clean.

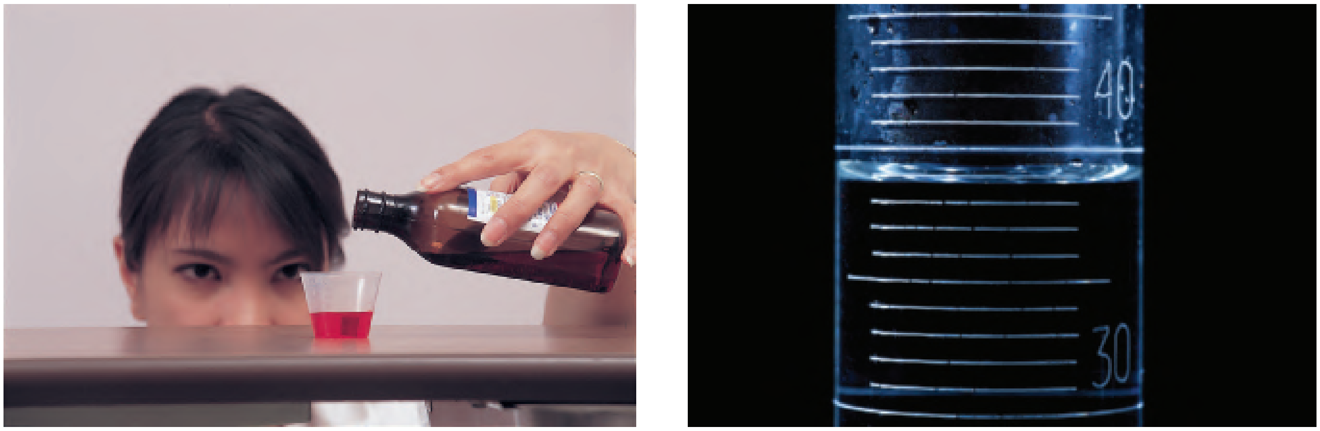
Note

In some areas a physician's order is required for pill crushing. If available, ask for the medication to be ordered in liquid or powdered form.

Preparation of Liquid Medications

Follow the “Guidelines for Administration of Oral Medications” at the beginning of this section. Preparation of *liquid medications* requires these additional steps:

1. Shake the bottle if indicated. Remove the cap and place it upside down on the table.
2. Hold the medicine bottle with the label side upward to prevent smearing of the label while pouring (Figure 8-6).
3. While holding the medicine cup straight at eye level, pour the prescribed amount of medication. Measuring should be to the bottom of the **meniscus** (curve in the surface of the liquid) (Figure 8-6).
4. Replace the cap on the bottle.
5. Compare the information on the medication sheet against the label on the stock bottle and the quantity of drug in the cup.
6. Replace the medication bottle in the cupboard or the medicine cart.
7. Recheck the Seven Rights of Medication Administration.
8. Proceed with the “Guidelines for Administration of Oral Medications.”



ggw/Shutterstock.com.

Figure 8-6 (A) Hold the medicine bottle with label side up and medicine cup at eye level. (B) Measure to the bottom of the meniscus.

When administering liquid medication to someone who is unable to drink from a cup (e.g., infants and persons with wired jaws), a syringe may be used. Follow the “Guidelines for Administration of Oral Medications.” Administration of *liquid medications orally via syringe* requires these additional steps:

1. Pour the prescribed medication into the medicine cup. If automated, scan it and compare the label against the medication sheet or automated screen for the Seven Rights of Medication Administration: right medicine, right amount, right time, right route, right patient, right technique, and right documentation.
2. Withdraw the prescribed amount with a syringe.
3. Check the medication and order using the Seven Rights of Medication Administration.
4. Identify the patient and scan wristband if using an eMAR, verify name and date of birth (DOB), and elevate the patient’s head.

Note

Never mix two liquids together in the same medicine cup. When pouring medication, never touch the medicine cup with the medication bottle. If too much medication is poured into the medicine cup, discard the extra medication. Do not pour the extra medication back into the bottle.

5. Be sure the patient is alert and able to swallow.
6. Place the syringe tip in the pocket between the cheek and the gums. (When administering large amounts of liquid via a syringe, it helps to fit a 2-inch length of latex tubing on the syringe tip to facilitate instillation of the medication into the cheek pocket.)
7. Instill the medication slowly to lessen chances of aspiration.
8. Be sure the patient swallows all the medication completely.
9. Proceed with "Guidelines for the Administration of Oral Medications."
10. Remember to document appropriately.

Liquid oral medication is the preferred form for children younger than 5 years old. In addition, flavored medications are often preferred and better tolerated by young children.

Administration of Medications Rectally

Medications are sometimes ordered to be administered by the rectal route. This route is used for small children who cannot swallow medication, comatose patients, or those who cannot swallow pills whole. It can also be used in patients with nausea or vomiting. The **rectal medication** may be in suppository form or in liquid form to be administered as a retention enema. This treatment is more effective with the patient's cooperation. Tact and consideration are required for successful administration of rectal medications. Remember to respect the patient's dignity and privacy by closing the door and curtains completely. Do not expose the patient unnecessarily.

The **retention enema** is administered in the same way as a cleansing enema. However, the retention enema must be retained approximately 30 min or more for absorption of the medication. Therefore, the patient is instructed to lie quietly on either side to aid in retention. If the patient is uncooperative, is unconscious, or has poor sphincter control, the buttocks can be taped together with 2-inch paper adhesive for 30 min. Do not use this method unless absolutely necessary. Remember to treat the patient with dignity. Always explain everything you are doing and why. Even if patients are unconscious or unable to speak, they may be able to hear and cooperate in some way if they understand.

Clinical Application

Patient Education of Suppositories

When a patient receives a medication for self-administration at home it is very important to ensure that you educate them on the route of administration. Although to a health care professional this may seem arbitrary, many times patients or their family members who are caring for them assume all medications are to be taken orally. This would of course be a problem if the prescribed medication is a suppository meant to be administered per rectal. Common suppositories that are prescribed for self-administration are hydrocortisone suppositories used for hemorrhoids and acetaminophen suppositories used for pain and fever. Ensure that the patient understands that the suppository needs to be unwrapped prior to administration. Although this may seem like common sense, it may not be. To be safe, always assume that the patient needs as much information as you can provide.

Administration of Rectal Suppository

1. Wash hands.
2. If using an eMAR, scan and compare the label against the medication sheet or screen. Check the medication order using the Seven Rights of Medication Administration.
3. Identify the medication (purpose, side effects, contraindications, cautions, and normal dose range). Research information, if necessary.
4. Assemble supplies: disposable gloves and water-soluble lubricant.
5. Select the medication as ordered, checking medication name and dosage again. Some suppositories are stored in a refrigerator, and some may be stored at room temperature, according to the manufacturer's instructions.
6. Check the patient's identification bracelet and, if automated, scan the patient's wristband, ask the patient for name and DOB, and explain the procedure. Answer any questions.
7. Close the door and curtain completely.
8. Lower the head of the bed if necessary and position the patient on the left side with the upper knee bent. Keep the patient covered, exposing only the rectal area (Figure 8-7).
9. Put on disposable gloves.
10. Remove the suppository from the wrapper and lubricate the tapered end with a water-soluble lubricant.
11. With the nondominant hand, separate the patient's buttocks gently to reveal the anus.
12. Ask the patient to take a deep breath. Insert the lubricated suppository gently into the rectum and push gently with gloved index finger until the suppository has passed the internal sphincter (Figure 8-8). With infants, use the gloved *little* finger.

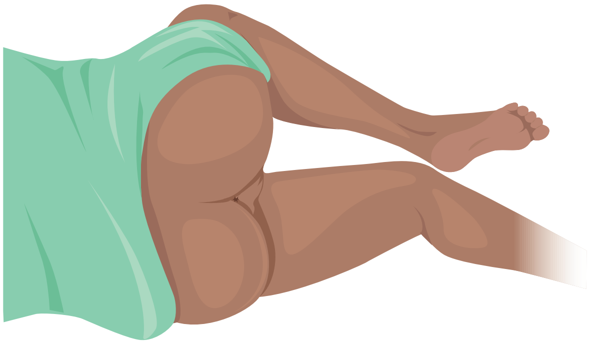


Figure 8-7 Drape and position patient on side with upper knee bent.

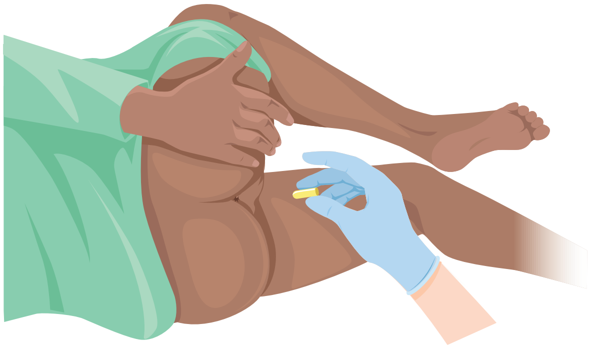
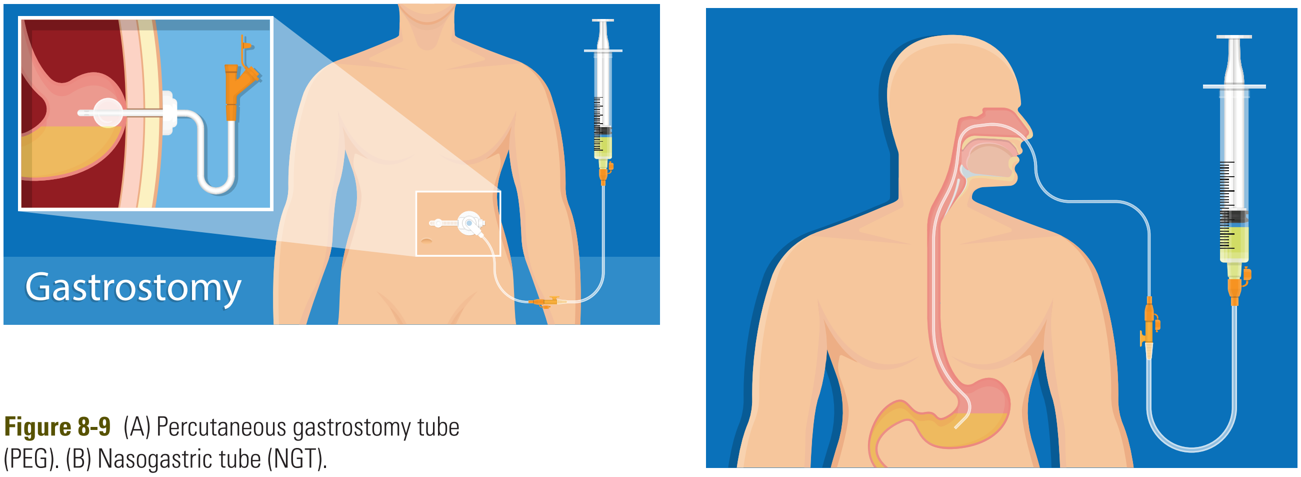


Figure 8-8 Lubricate tip of suppository and insert it with covered index finger. Push the suppository past the sphincter.

13. Urge the patient to retain the suppository for at least 20 min. If the patient is unable to cooperate, hold the buttocks together as required.
14. Remove and dispose of gloves, turning them inside out as you remove them.
15. Be sure the patient is comfortable, with covers and bed adjusted appropriately.
16. Wash hands.
17. Record the medication in the appropriate place.

Administration of Medications by Percutaneous Endoscopic Gastrostomy (PEG) or Nasogastric Tube (NGT)

A PEG or NGT is not inserted solely for the purpose of administering medication (refer to Figure 8-9). However, medications are sometimes ordered by this route when a PEG or NGT is in place for tube feeding or for suction. When medications are ordered by PEG or NGT, follow the "Guidelines for Administration of Oral Medications" and "Preparation of Liquid Medications." Typically, NGT and PEG tube administration is not in the scope of practice for medical assistants. Always check with your licensing body.



rumruay/Shutterstock.com.

rumruay/Shutterstock.com.

Figure 8-9 (A) Percutaneous gastrostomy tube (PEG). (B) Nasogastric tube (NGT).

Percutaneous endoscopic gastrostomy (PEG) tube medication administration or **Nasogastric tube (NGT) medication administration** requires these additional steps:

1. Check the medication order using the Seven Rights of Medication Administration. If using an eMAR, scan it and compare the label against the medication sheet or automated screen.
2. If the medication must be administered on an empty stomach and the patient is receiving a tube feeding, hold the medication, stop the tube feeding for 30–60 min depending upon the medication being administered, and return at the appropriate time to administer the medication.
3. If the patient is not receiving a tube feeding or the medication can be administered with the tube feeding, continue with medication administration.
4. Wash hands. Wear gloves when handling tubes.
5. Prepare the medication as ordered and take it to the patient's room. Be sure the medication is at room temperature.
6. Check the identification bracelet and, if automated, scan the patient's wristband, ask the patient their name and DOB and verify it, and explain the procedure. Elevate the head of the bed, if not contraindicated.
7. Hold the end of the tube up and remove the clamp, plug, or adapter.
8. Verify that the tube is properly placed in the stomach and verify that the tube is taped at the appropriate centimeter marking. Aspirate with bulb or piston syringe for stomach contents and check the pH of the aspirated fluids. Gastric juice is acidic (pH of 0.9–1.5). If the aspirate does not meet these parameters or if there is any question, *do not* instill any liquids. Instead, report to the person in charge. If the criteria are met, flush the tube with normal saline solution or with water.
9. Clamp the tube with your fingers by bending it over upon itself or by pinching it. After the tube is closed, remove the plunger or the bulb from the syringe, leaving the syringe attached firmly to the tubing. Flush the tube with water.
10. Pour the medication into the syringe. Release or unclamp the tubing and let the medication flow through by gravity. Never force fluids down a nasogastric tube. Watch the patient during the procedure and stop immediately at any sign of discomfort, coughing, or shortness of breath by pinching the tube. Holding the syringe too high causes fluid to run in too quickly, possibly causing nausea and vomiting. The syringe should be at the level of the patient's shoulder.
11. Before the syringe empties completely, flush the tube by adding 60–100 mL of water to the syringe or the amount ordered. If the patient's input and output are being monitored, be sure to add this amount to the patient's record.

12. After the water has run in, pinch the tube, remove the syringe, and clamp or plug the tube. If the patient is ordered suction, be sure to leave the suction turned *off* for at least 30 min until the medication is absorbed, then restart suction as ordered. If the patient is receiving a tube feeding, be sure to leave the tube feeding turned *off* for 30–60 min, depending upon the medication, until the medication is absorbed; then restart the tube feeding.
13. Position the patient on the right side and/or elevate the head of the bed to encourage the stomach to remain empty. Make the patient comfortable.
14. Proceed with "Guidelines for the Administration of Oral Medications" for documentation.

Chapter Review Quiz

1. Name three advantages and three disadvantages of oral administration compared with administration by injection.

____

____

____

____

____

____

Match the column on the left with the appropriate action on the right. Actions may be used more than once.

2. ____ To facilitate swallowing
3. ____ If NPO for laboratory tests
4. ____ Patient vomits 15 min after
5. ____ Most medications
6. ____ Patient is allergic to penicillin
7. ____ Most important medicine
8. ____ Tablet cannot be swallowed
9. ____ Sustained-release capsules
10. ____ Dilantin ordered PO, patient NPO for surgery

a. Watch closely for drug reactions
b. Crush tablet, mix with applesauce
c. Administer first
d. Usually cannot be opened
e. Elevate patient's head
f. Notify person in charge
g. Modify schedule, give medicine later
h. Administer with water
i. Leave medication at bedside

Complete the following statements by filling in the blanks.

When pouring liquid medicine:

11. The bottle should be held ____.

12. The medicine cup should be held ____.

13. The bottle cap should be placed ____.

14. If medication is in suspension, the bottle should first be ____.

When administering medication by nasogastric tube:

15. Check tube placement first with which two tests:

____

____

Check the appropriate answer.

When administering medication by PEG or nasogastric tube:

16. ___ **a.** Medication should be pushed through the tube by pressure on the barrel of a syringe.

___ **b.** Medication should flow through the tube by gravity.

17. ___ **a.** Medication should be cold.

___ **b.** Medication should be at room temperature.

18. ___ **a.** Patient's head should be elevated.

___ **b.** Patient should be placed in the Trendelenburg position.

19. Name four steps in the administration of a rectal suppository that are different from PO administration.

____

____

____

____

20. Medication documentation should include:

____

____

____

____

Checklist for Administration of Oral Medications

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked medication sheet/automated screen for date, dosage, time, route, and allergies	______	______
3. Identified medication: purpose, side effects, contraindications, cautions, interaction, and normal dosage range	______	______
4. Selected appropriate medicine cup	______	______
5. Selected correct medication/scanned barcode and checked label against medication sheet for Seven Rights of Medication Administration	______	______
6. Calculated correct dosage on paper if necessary and verified calculations with instructor	______	______
7. Placed medication as ordered in cup without opening packet or touching medication; prepared liquid medication by shaking if necessary, pouring away from label and measuring at eye level	______	______
8. Identified patient by checking/scanning bracelet and asking patient for name and DOB; used alternate method for verifying identity if necessary; to prevent aspiration, make sure head of bed is elevated unless otherwise ordered	______	______
9. Explained procedure to patient and answered any questions about medication	______	______
10. Checked patient's vital signs if necessary for specific medicine	______	______
11. Opened unit-dose packages and offered medication in container to patient	______	______
12. Provided drinking water and assisted patient as necessary	______	______
13. Made patient comfortable and left unit in order	______	______
14. Recorded medication, dosage, time, and signature or initials on patient's record	______	______

Note: S, satisfactory; U, unsatisfactory.

Checklist for Administration of Rectal Suppository

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked the medication order for date, dosage, time, route, and allergies	______	______
3. Identified medication: purpose, side effects, contraindications, cautions, and normal dosage range	______	______
4. Assembled supplies: gloves and lubricant	______	______
5. Selected/scanned correct medication and checked label with medication order for Seven Rights of Medication Administration	______	______
6. Identified patient by checking bracelet or scanning and asking patient for name and DOB; used alternate method for verifying identity if necessary	______	______
7. Explained procedure to patient and answered any questions about medication	______	______
8. Closed door and curtain	______	______
9. Positioned patient on left side with upper knee bent and only rectal area exposed	______	______
10. Put on disposable gloves	______	______
11. Removed wrapping from suppository and lubricated tapered end	______	______
12. With nondominant hand, separated buttocks gently	______	______
13. Instructed patient to take a deep breath and inserted suppository gently, pushing it past the sphincter	______	______
14. Instructed patient about retaining the suppository	______	______
15. Removed gloves correctly and disposed of them appropriately	______	______
16. Made patient comfortable and left unit in order	______	______
17. Washed hands	______	______
18. Recorded medication, dosage, time, and signature or initials on patient's record	______	______

Note: S, satisfactory; U, unsatisfactory.

Chapter 9

Administration by Parenteral and Other Routes

Key Terms and Concepts

Bolus
Buccal administration
Continuous IV infusion
Dry-powder inhalers (DPIs)
Inhalation route
Injections
Intermittent IV infusion
Intradermal
Intramuscular
Local effects
Metered-dose inhalers (MDIs)
Parenteral
Piggyback
Push
Small-volume nebulizer (SVN)
Subcutaneous
Sublingual administration
Systemic effects
Topical
Transcutaneous
Transdermal
Z-track method

Objectives

Upon completion of this chapter, the learner should be able to:

1. Name four administration routes with systemic effects.
2. Explain administration via the sublingual and buccal routes, including instructions to the patient.
3. Demonstrate application of transcutaneous medications.
4. Compare and contrast the advantages and disadvantages of the inhalation route.
5. Describe patient education for those receiving inhalation therapy with hand-held nebulizers.
6. Contrast small-volume nebulizers (SVNs), metered-dose inhalers (MDIs), and dry-powder inhalers (DPIs).
7. Identify the parts of a syringe and needle.
8. Select appropriate length and correct gauge needles for various types of injections.
9. List the three types of syringes and their purposes.
10. Demonstrate drawing up medications from a vial and an ampule.
11. Describe an intradermal injection.
12. Describe a subcutaneous injection.
13. Describe three sites for intramuscular (IM) injection.
14. Describe an IM injection.
15. Give the purpose and a demonstration of Z-track injection.
16. Explain IV administration and various types of IV fluids that can be prescribed.
17. Identify three local routes of administration.

Parenteral routes include any route other than the oral route. However, the term *parental* has evolved to mean any means of injection that bypasses the skin and mucous membranes. The other routes that must be considered besides the "injectables" are:

- The skin (transdermal route)
- Mucous membranes (sublingual and buccal routes)
- Eyes and ears (otic and optic routes)
- Respiratory tract (inhalation route)

The chosen route of administration of a medication can be understood more easily if the *purpose* of administration or the effects desired are considered in two categories: systemic and local. **Systemic effects** are those affecting the body as a whole, the entire system. The goal of administering drugs for systemic effects is to distribute the medication through the circulatory system to the area requiring treatment. Routes with systemic effects include (1) sublingual or buccal, (2) transcutaneous (transdermal), (3) inhalations, and (4) injections.

Local effects are those limited to one particular part (location) of the body with very little effect (if any) on the rest of the body. Medications in this category include:

1. Medications applied to the skin for skin conditions, sometimes called **topical** medications
2. Drugs applied to the mucous membranes to treat that specific tissue
3. Medications instilled in the eyes for eye conditions
4. Medications instilled in the ears for ear conditions

Sublingual and Buccal Administration

With **sublingual administration**, the medication is placed under the tongue. The drug is absorbed directly into the circulation through the numerous blood vessels located in the mucosa of this area. With **buccal administration**, the medication is placed in the pouch between the cheek and the gum at the back of the mouth. The sublingual route is used more commonly than the buccal. Medications absorbed in this way are unaffected by the stomach, intestines, or liver. Absorption via this route is quite rapid, and therefore, this method is used frequently when a quick response is required (e.g., with nitroglycerin to treat acute angina pectoris). The constricted coronary blood vessels are usually dilated within a few minutes, bringing quick relief from pain.

Patient Education

For the sublingual or buccal route, include the following instructions:

1. Hold the tablet in place with mouth closed until the medication is absorbed.
2. Do not swallow the medication.
3. Do not drink or take food until the medication is completely absorbed (~15 min).

Transcutaneous Drug Delivery System

Transcutaneous, or **transdermal**, systems deliver the medication to the body by absorption through the skin. Nitroglycerin ointment, for example, is applied to the skin in prescribed amounts every few hours for prevention of angina pectoris (chest pain). The absorption is slower, and therefore this method is not effective in the treatment of acute angina attacks. Other transcutaneous delivery systems utilize a patch impregnated with a particular medication, applied to the skin, and left in place for continuous absorption. Examples of transcutaneous drug delivery systems include nitroglycerin (Nitro-Dur), in which the patch is sometimes left in place for 12 h daily (e.g., put on in the morning and removed at night to reduce development of nitrate tolerance) for treatment of chronic angina; scopolamine (Transderm-Scop), in which the patch is placed behind the ear and left in place for up to 72 h, as necessary, to prevent motion sickness; and fentanyl (Duragesic), applied on the skin and changed every 72 h in the management of chronic pain in patients requiring opiate analgesia. Other medications delivered transdermally include estrogen (Climara), nicotine replacement for smoking cessation therapy, and birth control (Ortho Evra). Absorption by this method is slower, but the action is more prolonged than with other methods of administration; and most important, the drug is released at a constant rate so that the concentration of the drug in the body is kept at a certain level.

Note

To reduce the occurrence of headaches, sometimes the physician will order the nitroglycerin ointment or patch to be applied at bedtime and removed the next day at noon.

Clinical Application

Medication patches such as fentanyl (Duragesic) must be disposed of properly because they still contain medication when removed. In the acute care setting, the health care professional must verify the patch is in place once per shift. When removing the patch to place a new one, they must have a witness to the disposal. They should be folded in half and disposed of in a designated area such as a “sharps” container that cannot be re-accessed. When educating a patient about disposal at home, warn patients that the discarded patch can be dangerous to children and animals if it is handled or chewed. Abuse-deterrent disposal systems are also available for at-home disposal of patches (as well as other dosage forms).

Patient Education

For those applying transcutaneous systems of administration, include the following instructions. With nitroglycerin ointment (Figure 9-1):

1. Squeeze the prescribed amount of ointment onto dose-measuring application paper (Appli-Ruler). When the ointment reaches the correct marking, give the tube a slight twist to cut off the ointment. Then recap the tube.
2. *Do not* touch the ointment! Absorption of ointment through the skin of the fingers can cause a severe headache. Wearing gloves eliminates this risk.
3. Carefully fold the Appli-Ruler paper lengthwise with the ointment inside.
4. Flatten the folded paper carefully to spread the ointment inside. *Do not* allow the ointment to reach the edges of the paper. Keep the paper folded.
5. Rotate the sites for application. Appropriate areas include chest, back, upper arms, and upper legs. *Do not* shave the area. Be sure the area is: 1) clean; 2) dry; and 3) free of irritation, rash, and abrasion.
6. After the area for application is exposed, open the paper carefully and apply paper to the skin, ointment side down. *Do not* touch the ointment. Fasten paper in place with paper tape. Write the date, time, and your initials on the tape.

7. Remove the previous paper carefully, without touching the inside, and discard it in the trash container. Cleanse the area and inspect the skin for any sign of irritation. Report and record any skin changes.
8. Wash hands immediately.
9. Report and record any skin changes or complaints of headache.

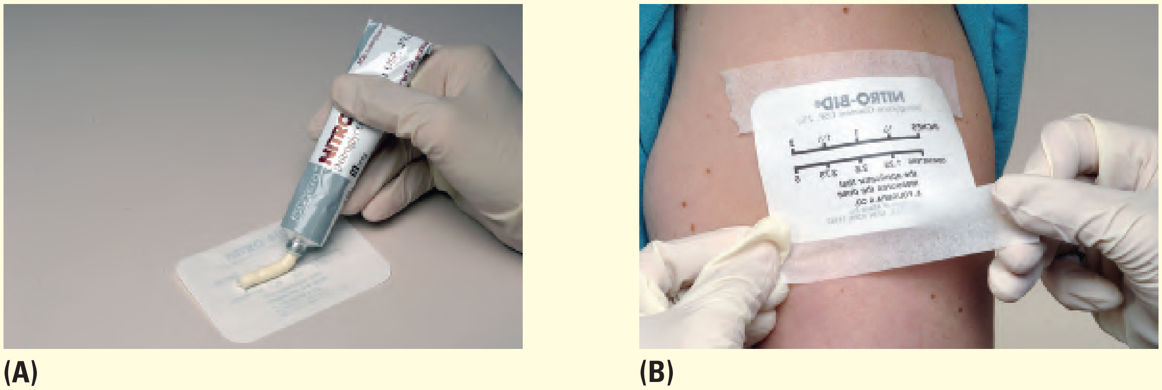


Figure 9-1 Transdermal administration of nitroglycerin ointment. (A) Ointment is measured on Appli-Ruler paper. (B) Paper containing ointment is applied to the skin and fastened with paper tape. Write date and time on tape.

With transdermal sealed drug delivery systems (Figure 9-2):

1. Remove the previous patch carefully, without touching the inside, and discard it in the designated container. Cleanse the area and inspect the skin for irritation.
2. Select site for new administration, rotating areas. Be sure the skin is clean, dry, and free of irritation.
3. Open the packet carefully, pulling the two sides apart *without touching the inside.*
4. Apply the side containing the medication to the skin. Press the adhesive edges down firmly all around. If for any reason the adhesive edges do not stick, fasten in place with paper tape. This is usually unnecessary. Write date, time, and initials on the patch.
5. Wash hands immediately.
6. To prevent burns to the patient, certain patches must be removed prior to cardioversion or defibrillation. Also, removal of certain patches (e.g., Catapres-TTS) before undergoing magnetic resonance imaging (MRI) is recommended because the patches contain aluminum.

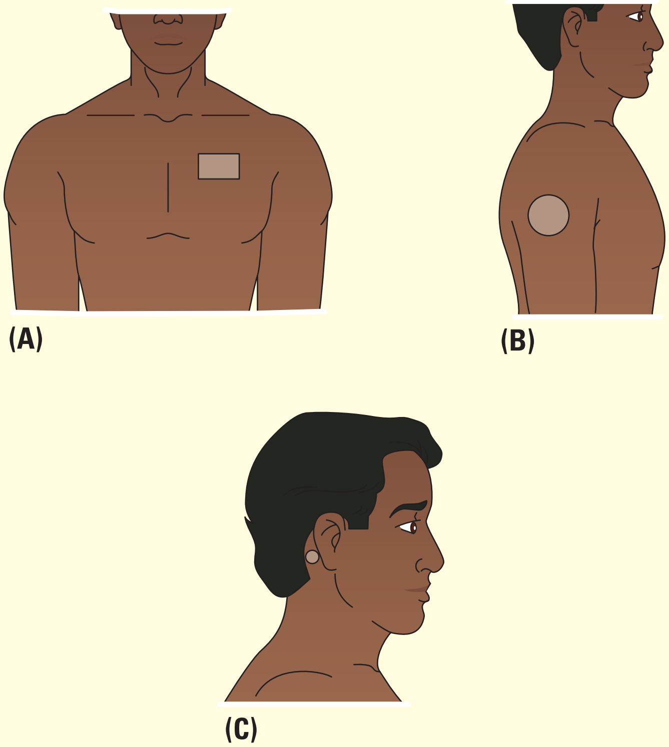
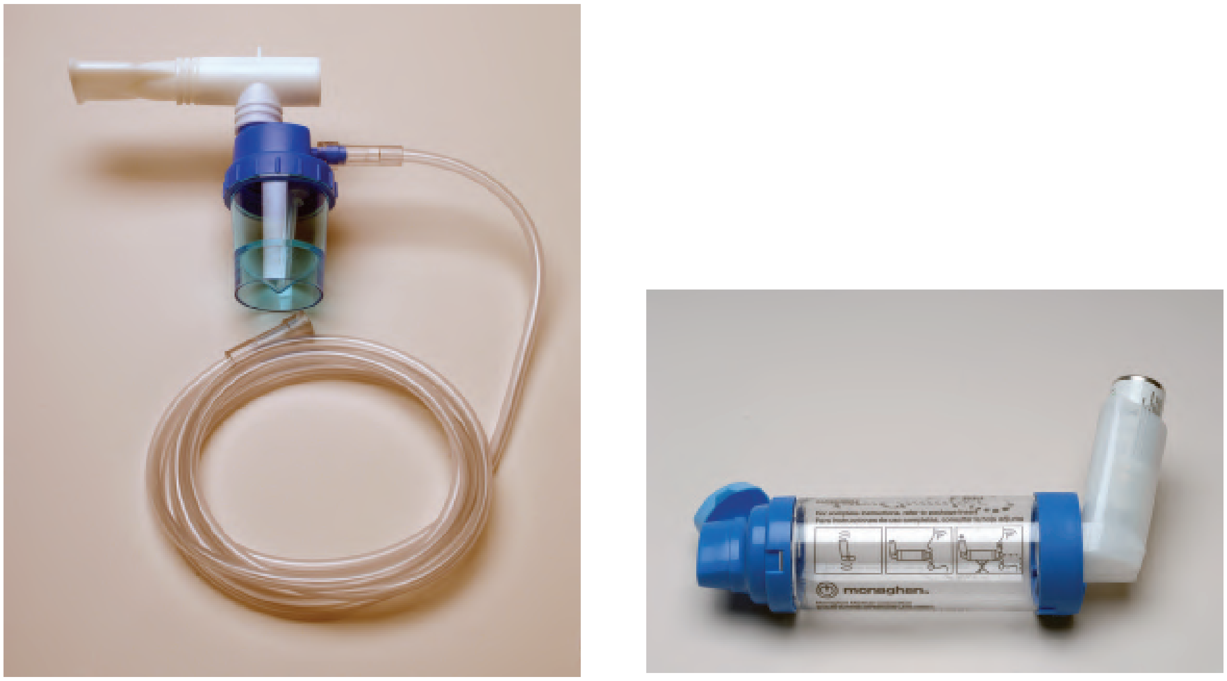


Figure 9-2 Transdermal drug delivery. Dermal patches vary in size and shape. (A, B) For prevention of angina pectoris. (C) For prevention of motion sickness. Other patches are also available for analgesia, estrogen replacement, and smoking cessation.

Inhalation Route

Medications are frequently administered by the inhalation route, especially to those with chronic pulmonary conditions, such as asthma. Patients may self-administer the medication with a metered-dose inhaler (MDI), dry-powder inhaler (DPI), or small-volume nebulizer (SVN) (Figure 9-3), or the physician may prescribe inhaled medications to be administered by trained personnel such as respiratory therapists.



(A) **(B)**

Figure 9-3 (A) Small-volume aerosol nebulizer (SVN). (B) Metered-dose inhaler (MDI) with spacer.

Advantages of the **inhalation route** include:

1. Rapid action of the drug, with local effects within the respiratory tract
2. Potent drugs may be given in small amounts, minimizing the side effects
3. Convenience and comfort of the patient

Disadvantages of inhalation therapy include:

1. Requires cooperation of the patient in proper breathing techniques for effectiveness.
2. Adverse systemic side effects may result rapidly because of extensive absorption capacity of the lungs.
3. Improperly administered, or too frequently administered, inhalations can lead to irritation of the trachea or bronchi, or bronchospasm.
4. Patients with asthma and chronic obstructive pulmonary disease (COPD) sometimes become dependent on an SVN, a DPI, or an MDI.
5. If not cleaned properly, the SVN can be a source of infection.

Metered-Dose Inhaler (MDIs)

Metered-dose inhalers (MDIs) (refer to Figure 9-3B) deliver a measured (metered) dose via a propellant within a canister. MDIs are portable and easy to use; however, proper administration by the patient is essential for drug effectiveness. Older adult patients may have difficulty coordinating the depression of the canister and inhaling at the same time. A *spacer* may be added to act as a reservoir for the aerosol, allowing the patient to first depress the canister and then inhale. Many spacers have an audible horn or whistle to signal the patient if inspiration is too rapid. MDIs may be used in pediatric patients with a mouthpiece or a mask. A full MDI canister provides approximately 200 puffs of medication.

Patient Education

How to Use a Metered-Dose Inhaler (MDI)

1. Sit upright or stand.
2. Assemble the inhaler and shake for 10 seconds. (For consistent dosing, it is recommended to discharge a waste dose if it has been 14 days since you last used your inhaler.)
3. Remove the upper dentures if dentures are loose.
4. Exhale slowly and completely.
5. Place the mouthpiece between the lips, forming a seal, or—preferably—use a spacer prescribed by your physician.
6. Push down on the inhaler while breathing in slowly and deeply to full capacity.
7. Hold your breath for at least 5–10 seconds.
8. Exhale slowly through pursed lips.

If your prescription is for more than one puff, rest for 1 or 2 min before the second dose.

Note: If a bronchodilator and an inhaled steroid medication are to be given at the same time, administer the bronchodilator first and then the steroid.

Important: If using an inhaled steroid (such as Asmanex, Flovent, Pulmicort, or QVAR), rinse your mouth out with a mouthwash or water and spit it out after using the inhaler to reduce risk of developing an oral fungal infection such as thrush.

Small-Volume Nebulizers (SVNs, MINI-NEBs, MED-NEBs)

Many drugs for the respiratory system may be delivered in aerosol form via a **small-volume nebulizer (SVN)** (refer to Figure 9-3A). The nebulizer is powered by a gas source, usually a small air compressor in the home care setting. For optimal drug deposition in the lungs, proper breathing techniques must be used by the patient. The patient should be instructed to inhale slowly and deeply, perform a short breath hold, and exhale slowly. In addition to the side effects of the drugs, patients should be cautioned that dizziness may occur if they hyperventilate (breathe too rapidly). Proper cleaning of equipment daily is essential to avoid infection.

Patient Education

Proper Home Cleaning of Small-Volume Nebulizers

1. Disassemble the pieces of the nebulizer. Wash in mild soapy water and rinse thoroughly.
2. Place in a solution of one part vinegar to two parts water. Soak for 20–30 min.
3. Wash your hands with soap and water.
4. Remove the nebulizer parts from the vinegar solution and rinse with warm tap water.
5. Allow to dry completely.
6. Reassemble pieces for next use.

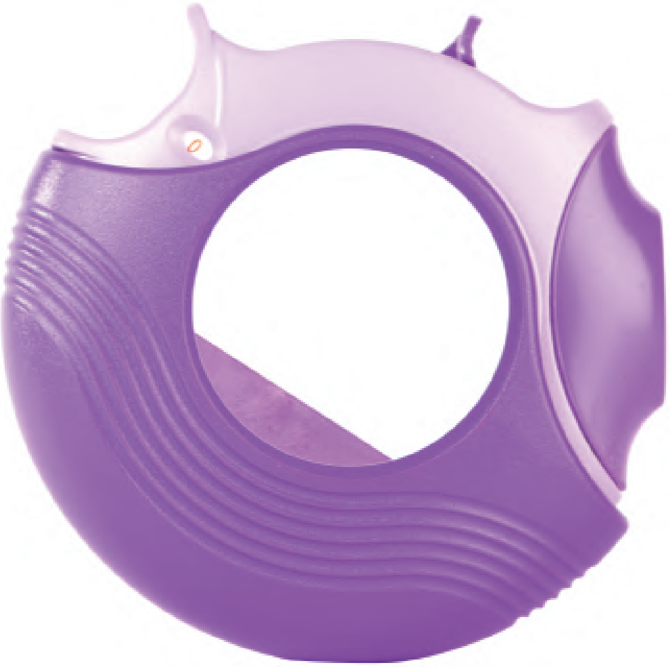
Patient Education

With use of an inhaler or nebulizer, include the following instructions:

1. Name of the medication, dosage, and how often it is to be administered.
2. Desired effects and possible adverse side effects (e.g., palpitations, tremor, nervousness, dizziness, headache, nausea, dry mouth, irritated throat, hoarseness, or coughing).
3. Notify the physician if any adverse side effects occur or if the medication seems ineffective. The physician may want to change the dosage or the medication.
4. *Do not* to take any other medication, including over-the-counter drugs, without the physician's permission. Many drugs and alcohol can interact with these drugs, causing serious side effects.
5. Rising slowly from a reclining position will help prevent dizziness.
6. Rinse the mouth before inhalation to moisten the mouth.
7. Rinse the mouth after inhalation to counteract dry mouth or unpleasant taste and spit the water out; do not swallow.
8. Step-by-step demonstration with the patient, answering all questions.
9. Rinse equipment after use and storage of medication as indicated on the package.
10. Importance of not smoking.
11. Importance of handwashing before treatments.

Dry-Powder Inhalers (DPIs)

In recent years, **dry-powder inhalers (DPIs)** (Figure 9-4) have become popular to use, especially with children. DPIs are devices that deliver a drug in powder form into the lungs with no propellant or external power source. The patient must generate a sufficient inspiratory flow rate for the powder to aerosolize properly, and therefore DPIs are used for prophylactic treatment and not for acute breathing problems. The advantages of a DPI are that it is small and relatively easy to use, and it eliminates timing of inspiration technique problems encountered with an MDI. It also can be used in very cold environments such as ski slopes, where propellants may not work as effectively. The disadvantages are that a) fewer drugs are available in powder form, b) the patient must be able to generate a significant inspiratory effort for proper drug delivery and c) many contain lactose as an inactive ingredient.



khuntapol/Shutterstock.com.

Figure 9-4 One example of the many types of dry-powder inhalers (DPI).

Patient Education

How to Use a Dry-Powder Inhaler (DPI)

1. Sit upright or stand.
2. Break the dry powder capsule (if applicable) according to the device being used.
3. Remove the upper dentures if dentures are loose.
4. Exhale slowly and completely.
5. Place the mouthpiece between the lips, forming a seal.
6. Breathe in *quickly* and *deeply*.
7. Hold your breath for at least 5–10 seconds.
8. Exhale slowly through pursed lips.

Note: DPIs are *not* to be used in respiratory distress or emergency situations. The patient must be able to generate adequate inspiratory flow rates, and this device is used for maintenance or prophylactic treatment only.

Intermittent Positive Pressure Breathing (IPPB)

Intermittent positive pressure breathing treatments, although not commonly used, may be ordered by the physician. IPPB combines administration of an aerosol with a mechanical breather to assist patients who are unable to take a deep breath on their own. Health care professionals, such as respiratory therapists or nurses, are specifically trained in the use of this equipment.

Cautions with IPPB therapy include:

1. Monitor vital signs closely, watching for a sudden drop in blood pressure, tachycardia, and decreased or shallow respirations.
2. Observe for nausea or distended abdomen.
3. Watch for tremors or dizziness.
4. Assure the patient that coughing after the treatment is to be expected. The goal of the treatment is to aid in coughing up the loosened secretions.
5. Record the effectiveness of therapy and any side effects observed or reported by the patient.

Injections

To administer **injections**, you must be familiar with the equipment.

Syringes

The syringe has three parts (Figure 9-5):

1. ***Barrel.*** The outer, hollow cylinder that holds the medication. It contains the calibrations for measuring the quantity of medication. This portion is not sterile.
2. ***Plunger.*** The inner, solid rod that fits snugly into the cylinder. Pulling back on the plunger allows solution to be drawn into the syringe. Pushing forward on the plunger ejects solution or air from the syringe. The inner portion of the plunger is sterile.
3. ***Tip.*** The portion that holds the needle. Most tips have a system called a Luer-Lok, which locks the needle in place. The tip is sterile.

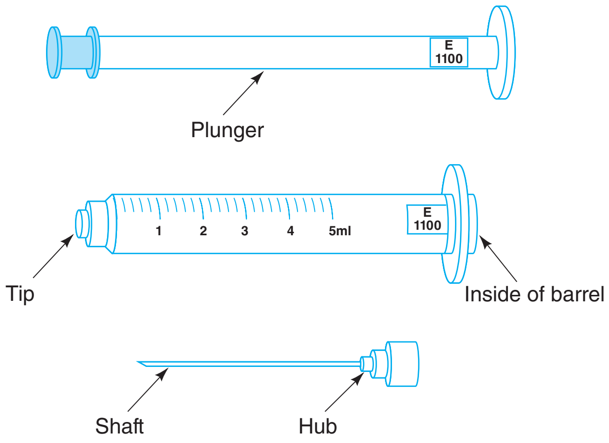


Figure 9-5 Parts of a syringe and needle that must remain sterile during preparation and administration of medication.

Most syringes are plastic and disposable after one use. Some syringes for special procedures are glass and must be resterilized after use.

Needles

The needle has three parts:

1. ***Hub.*** The flared end that fits on the tip of the syringe. This is sterile.
2. ***Shaft.*** The long, hollow tube embedded in the hub. Needles have shafts with different lengths. Shorter needles (1/2, 3/8, and 5/8 inches) are used for **intradermal** (into the skin) or **subcutaneous** (into the tissue just below the skin) injections. Longer needles (1½ and 2 inches) are used for **intramuscular** (into the muscle) injections. The length of the needle depends on the type of injection and the size of the patient (i.e., shorter needles for children and thin adults, and longer needles for larger adults). The gauge is the size of the lumen, or hole, through the needle, or the diameter of the shaft. The gauge is numbered in reverse order (i.e., the thinner needle with the smaller diameter has the larger number, for example, 25 gauge for subcutaneous injections, and 19–21 gauge, a thicker needle with a larger opening, for IM or IV injections). The size of the gauge is determined by the site of the injection and the viscosity of the solution (e.g., blood and oil require a thicker-gauge needle, e.g., 15–18). The shaft of the needle is sterile.
3. ***Tip.*** The pointed end with a beveled edge. The tip is sterile.

Three main types of syringes are used for injections. The type used is determined by the medication and the dosage. The three types are:

1. ***Standard syringe.*** Used most frequently for subcutaneous or IM injections, calibrated or marked in cubic centimeters (cc) or milliliters (mL) (Figure 9-6). The most commonly used size is 3 mL or 2½ mL. Larger sizes of 5–60 mL are available for other purposes (e.g., irrigations, withdrawing fluids from the body, and intravenous [IV] injections).

Copyright 2026 Cengage Learning. All
Editorial review has deemed that any suppre

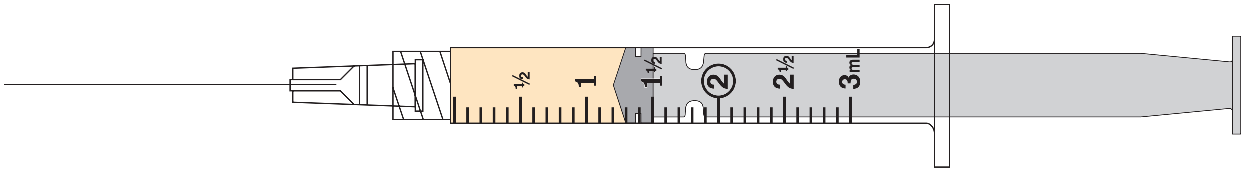


Figure 9-6 3-mL syringe.

2. ***Tuberculin (TB) syringe.*** Used for intradermal injections of very small amounts of a substance (e.g., testing for tuberculosis or for allergies). The TB syringe is also used for subcutaneous injections when a small amount of medication, up to 1 mL, is ordered (e.g., in pediatrics). The TB syringe is calibrated in tenths of a milliliter and holds only a total of 1 cc, or 1 mL (Figure 9-7).

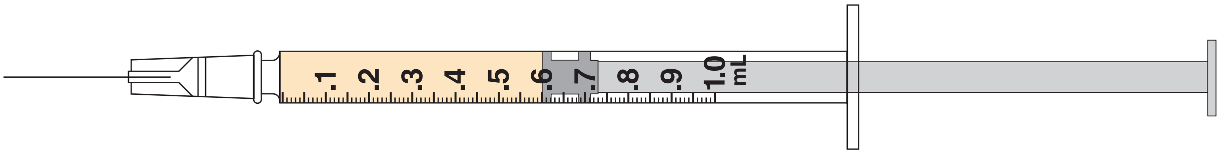
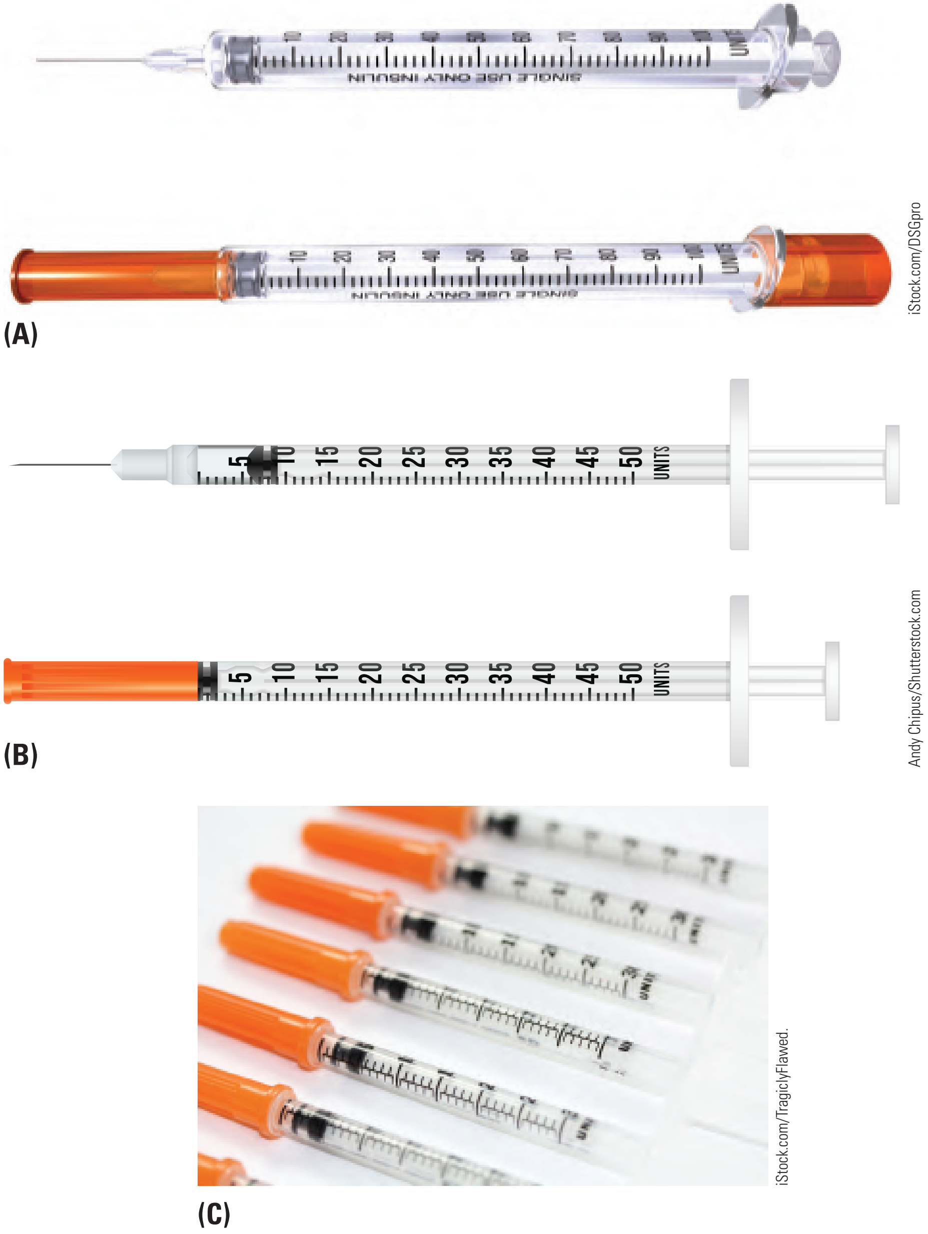


Figure 9-7 Tuberculin syringe with 1-mL capacity.

3. ***Insulin syringe.*** Used only for injection of insulin and calibrated in units. The size in common use today is U-100, in which 100 units of insulin is equal to 1 mL. The standard U-100 syringe has a dual scale: even numbers on one side and odd numbers on the other side. Look carefully at the calibrations on each side. Count each calibration (on one side only) as two units (Figure 9-8A). The insulin pen is another popular option for diabetics. There is a dial at the end in which you "dial in" the desired amount of insulin, which eliminates the need to withdraw insulin from a vial, thus limiting errors (Figure 9-9).

   There are also smaller insulin syringes to more accurately measure small amounts of insulin, such as for children (Figure 9-8B for Lo-Dose insulin syringes 50 units and 30 units). Look carefully at the calibrations. In these Lo-Dose syringes, each calibration counts *only one* unit. It is extremely important that you study the calibrations carefully each time you prepare for an insulin injection, to prevent a medication error from misinterpretation. **All insulin dosages should be double-checked by two caregivers before administration.**

   When instructing patients with newly diagnosed diabetes in self-administration or administration by a family member, be sure that they can see and understand the syringe calibrations and what they represent.



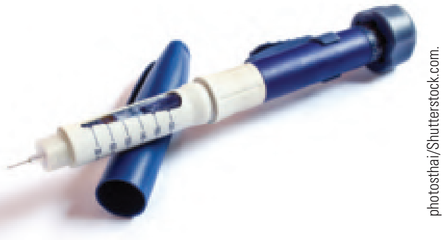
10 20 30 40 50 60 70 80 90 100 UNITS
SINGLE USE ONLY INSULIN
(A)
5 10 15 20 25 30 35 40 45 50 UNITS
(B)
(C)

iStock.com/DSGpro

Andy Chipus/Shutterstock.com

iStock.com/TragiclyFlawed.

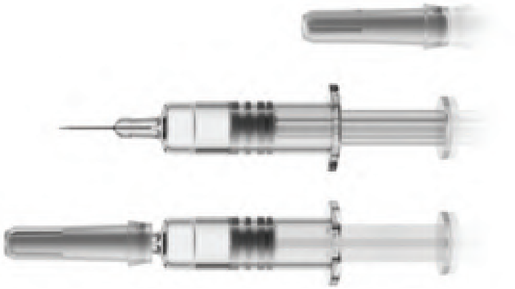
Figure 9-8 Insulin syringes. (A) Opposite sides of the same standard U-100 insulin syringe; note the numbers. (B) Opposite sides of the same Lo-Dose U-50 insulin syringe; note the numbers. (C) Lo-dose U-30 insulin syringes.



photosthai/Shutterstock.com.

Figure 9-9 Insulin pen.

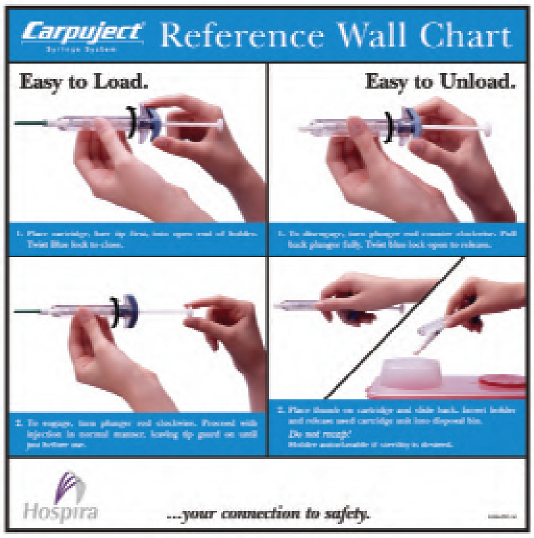
Prefilled syringes are available for certain medications (Figure 9-10). A premeasured amount of the drug is contained in the syringe. Check the dose ordered, compare with the dose in the syringe, and adjust if necessary. After injection, discard the syringe with needle attached and uncapped in the disposal bin.



Andrei Kuzmik/Shutterstock.com.

Figure 9-10 Prefilled, single-dose syringe. Courtesy of Roche Laboratories, Inc.

Prefilled cartridges are also available, in which a premeasured amount of a medication is contained in a disposable cartridge. These prefilled units are made ready for injection by placing the cartridge in a holder. This unit can then be used to access a needleless IV system, or a needle can be attached to administer IM or subcutaneous injections. After administration, the used cartridge is released from the holder and dropped into the disposal bin. If a needle is attached, it is released *uncapped* along with the cartridge into the bin. An example of such a unit is the *Carpuject*, which is produced by Hospira (Figure 9-11). Other units are also available. Follow the manufacturer's direction regarding assembly of the cartridge unit.


Carpuject Reference Wall Chart
Easy to Load.
Easy to Unload.
Hospira
...your connection to safety.

Carpuject Syringe System

Figure 9-11 Carpuject prefilled cartridge. Carpuject Syringe System.

Clinical Connection

Site Rotation

When administering a medication through the skin on a consistent basis, it is important to rotate administration sites. This is particularly important with insulin injections, transdermal patches, and topical creams and ointments. In all three cases, not rotating sites can lead to irritation and redness at the administration site. Insulin, if injected in the same spot repeatedly, can cause growths (fatty deposits) to form. These growths are undesirable for the patient and can affect the way insulin is absorbed. In the case of patches and topical preparations, not rotating sites can also lead to saturation of the skin by the medication, which changes its permeability, resulting in decreased absorption of the drug.

Drawing Up Medications

1. Wash hands.
2. Assemble equipment (i.e., syringe, needle, packaged alcohol wipes, and medication ampule or vial).
3. Check the order using the Seven Rights of Medication Administration. If there is an eMAR system in place, scan the patient and medication.
4. If the medication is contained in a vial, first remove the protective cap. Wipe the rubber diaphragm on top with an alcohol wipe. Check vial for date and discoloration of contents (Figure 9-12).
5. Seat the needle securely on the syringe by pressing firmly downward on the top of the needle cover. Pull the needle cover straight off. **Note:** Luer-Loks require a half-turn to lock the needle in place.
6. Draw air into the syringe equal to the amount of solution you will be withdrawing from the vial. Insert the needle into the center of the rubber diaphragm and inject air into the vial above the medication (Figure 9-13). Invert the vial and withdraw the prescribed dosage (Figure 9-14). Be sure the syringe is filled to the proper level with solution and no bubbles are present. Withdraw the needle from the vial. For IM injections, a small bubble (0.2 mL) of air may now be added to the correct dose of medicine already in the syringe.
7. The needle must now be recapped *carefully,* using only one hand, to maintain sterility and prevent needle sticks. After withdrawing the solution from an ampule or vial, the needle cap is laid horizontally on a flat surface. The syringe is held in the dominant hand, and the sterile needle is inserted carefully into the cap. The syringe with needle attached is then used to scoop up the cap without touching it. *Do not contaminate the needle* by touching it to the outside of the cap. Remember, *only sterile needles are to be recapped* (Figure 9-15). An alternative method would be to remove the needle from the syringe carefully and discard the needle in the sharps container, replacing it with a sterile, capped needle.
8. If the medication is contained in an ampule, use an ampule breaker to protect your fingers and break open along the scored marking at the neck. Tip the vial and withdraw the prescribed amount of medication. Recap the needle carefully according to previous directions. Use a filter needle to withdraw fluid from an ampule. Check the regulations in your area.

Note

If two drugs are to be combined in a syringe, you must first check for compatibility of the drugs.

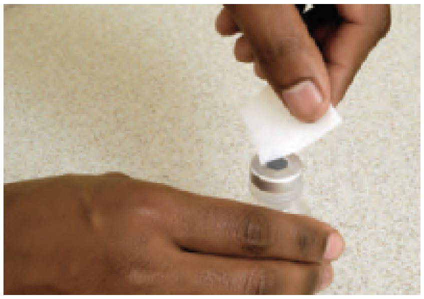


Figure 9-12 Preparing to withdraw medication from a vial. Cleanse the top with alcohol wipe.

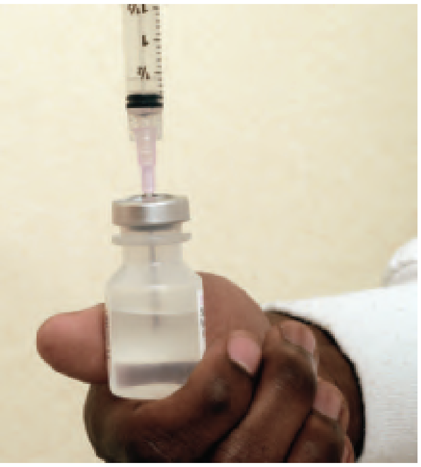


Figure 9-13 Injection of air into vial. Vial is upright so air is not injected into fluid.

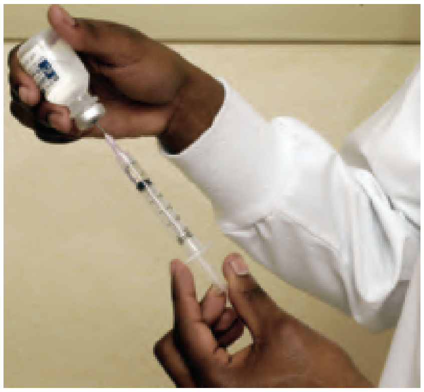


Figure 9-14 Withdrawal of prescribed amount of medication. Invert the vial. Be sure needle point is in fluid, not in the air.

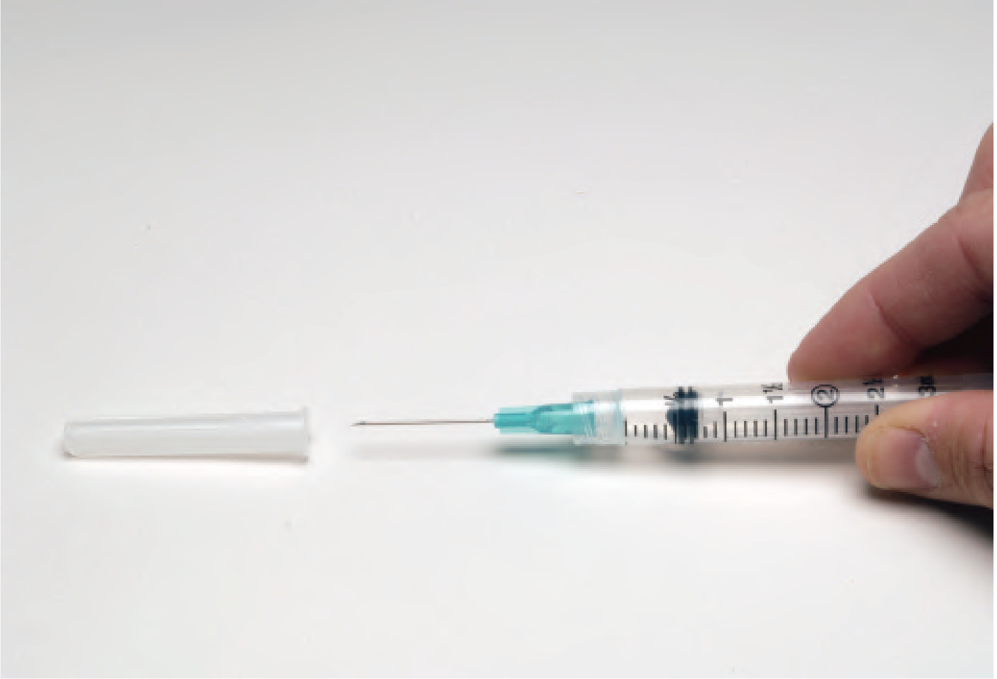
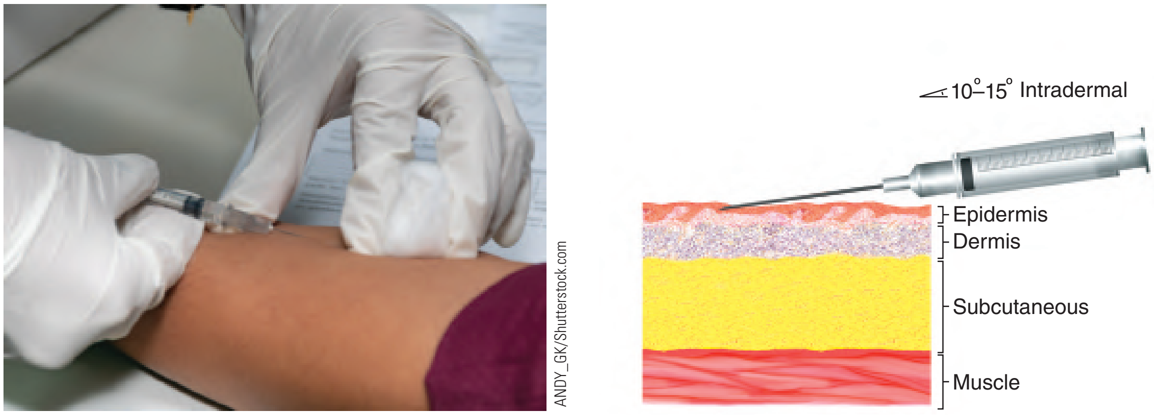


Figure 9-15 Recapping sterile needle. After withdrawing solution from an ampule or a vial, the needle cap is laid horizontally on a flat surface. The syringe is held in the dominant hand, and the sterile needle is inserted carefully into the cap. The syringe with needle attached is then used to scoop up the cap without touching it. Contaminated needles are never recapped; activate the safety feature and discard uncapped in a sharps container.

Administration by Injection

Intradermal injections are usually administered into the skin on the inner surface of the lower arm. For allergy testing, the upper chest and upper back areas may also be used. A small amount (0.1–0.2 mL) is injected so close to the surface that a wheal, or bubble, is formed by the skin expanding (Figure 9-16).



ANDY_GK/Shutterstock.com

Figure 9-16 Intradermal injection. Hold the arm in nondominant hand and stretch the skin taut. *The needle bevel is up*. The needle is almost flat against the arm. Inject slowly just under the skin so that a bubble forms.

The technique for intradermal injection is as follows:

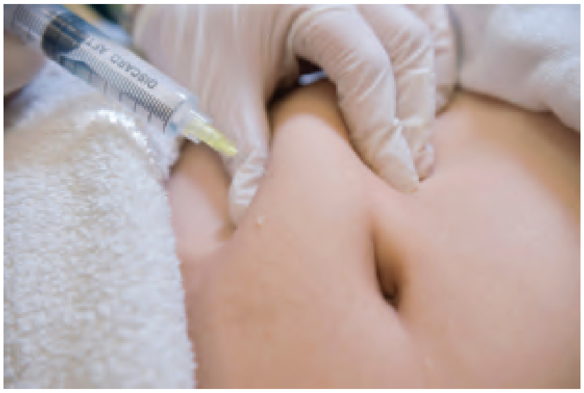
1. Wash hands.
2. Assemble equipment (i.e., TB syringe; 26 or 27 gauge, 3/8-inch needle; alcohol wipes; 2 × 2 gauze square; and medication).
3. Check the order using the Seven Rights of Medication Administration and draw up medication. If an eMAR system is in place, scan the patient and medication.
4. Identify the patient and explain the procedure. The arm should be supported on a flat surface.
5. Put on gloves.
6. Cleanse the skin with an alcohol wipe on the inner surface of the forearm (or other area if ordered by the physician). Allow the skin to dry thoroughly. *Do not* blow or fan the skin to assist drying because this can foster infection. (If you inject before the skin is dry, you might introduce alcohol into the skin and interfere with test results.) Avoid areas with hair or blemishes.
7. Hold the patient's arm in your nondominant hand and *stretch the skin taut*.
8. Hold the syringe so that *the bevel is up* and the needle is almost flat against the patient's arm. Slowly insert the needle only far enough to cover the lumen or opening in the needle. The point of the needle should be visible through the skin.
9. Inject the medication *very slowly*. You should see a small white bubble in the skin forming immediately. If no bubble forms, withdraw the needle slightly; it may be too deep. If the solution leaks out as you inject, the needle is not deep enough.
10. After the correct amount of medication is injected, withdraw the needle. *Do not* massage the area, or you may interfere with test results.
11. Activate the safety device and discard the syringe with needle *uncapped* into the sharps container immediately without touching the needle. Remove gloves. Wash hands.

12. Note drug name, dosage, time, date, and site of injection on the patient's record.
13. Instruct the patient not to scrub, scratch, or rub the area. Provide written instructions regarding the time to return for reading. Tell the patient to contact the physician immediately or report to an emergency facility if they experience breathing difficulty, hives, or a rash.

Caution

Do not start allergy testing unless emergency equipment is available nearby and personnel are trained in emergency care in case of anaphylactic response. Patients receiving allergy testing should remain in the office or clinical facility for 30 min after injection to be observed for possible anaphylactic reaction.

Subcutaneous injections are administered into the fatty tissues on the upper outer arm, front of the thigh, abdomen, or upper back (Figure 9-17). A 2½- to 3-mL syringe is usually used with a 24- to 26-gauge, ⅜- to ⅝-inch needle. No more than 2 mL of medication may be administered subcutaneously.



MDV Edwards/Shutterstock.com

Figure 9-17 Subcutaneous injection. The tissue is pinched, and the needle is held at a 45- to 90-degree angle.

Technique for subcutaneous injection is as follows:

1. Wash hands.
2. Assemble the equipment (correct-size syringe and needle, alcohol wipes, 2 × 2 gauze square, and medication).
3. Check the order with the Seven Rights of Medication Administration and draw up medication. If an eMAR system is in place, scan the patient and medication.
4. Identify the patient, ask the patient's name, check the armband, and explain the procedure. Use an alternate method to identify the patient if necessary.

5. If the patient is receiving frequent injections, be sure to rotate the injection sites.
6. Put on gloves.
7. Cleanse the skin with an alcohol wipe.
8. Pinch the skin into a fat fold of at least 1 inch (Figure 9-17).
9. Insert the needle at a 45- to 90-degree angle depending on the amount of subcutaneous tissue available. The leaner the patient, the closer to 45 degrees.
10. Inject the medication *slowly*, pushing the plunger all the way. An injection that is too rapid may cause pain.
11. Place a dry 2 × 2 gauze pad over the entry site, applying pressure with it as you withdraw the needle rapidly. Do not push down on the needle while withdrawing it. Do not massage the injection site.
12. Activate the safety device and discard the syringe with needle *uncapped* into the sharps container immediately.
13. Remove gloves and discard.
14. Wash hands.
15. Note the medication, dosage, time, date, site of injection, and your signature on the patient's record.
16. Observe the patient for effects and record observations.

Subcutaneous injection of heparin includes these steps:

1. Administer the heparin subcutaneously in the fat pad of the abdomen, at least 2 inches (approximately three fingers) away from the umbilicus. Use a ⅝- or ⅞-inch needle. Grasp the skin to form a fat pad, but do not pinch the tissues. Insert the needle with a dart-like motion at a 90-degree angle in the average size adult; in very thin patients a 45-degree angle may be used. Release fingers holding the fat pad and inject *slowly*.
2. Document the site of injection.
3. Do not massage the injection site. Merely hold the gauze on the site gently for approximately 10 seconds.
4. Be sure that there is no bleeding from the site.

IM injections are administered deep into large muscles (Figure 9-18). There are three recommended sites. Previously, there were two additional sites (dorsogluteal and rectus femoris) that are no longer recommended according to Centers for Disease Control and Prevention (CDC) guidelines owing to the close proximity of nerves and potential resultant nerve damage.

1. ***Ventrogluteal.*** Above and to the outside of the buttock area, on the hip
2. ***Deltoid.*** Upper outer arm above the axilla
3. ***Vastus lateralis.*** Front of the thigh toward the outside of the leg

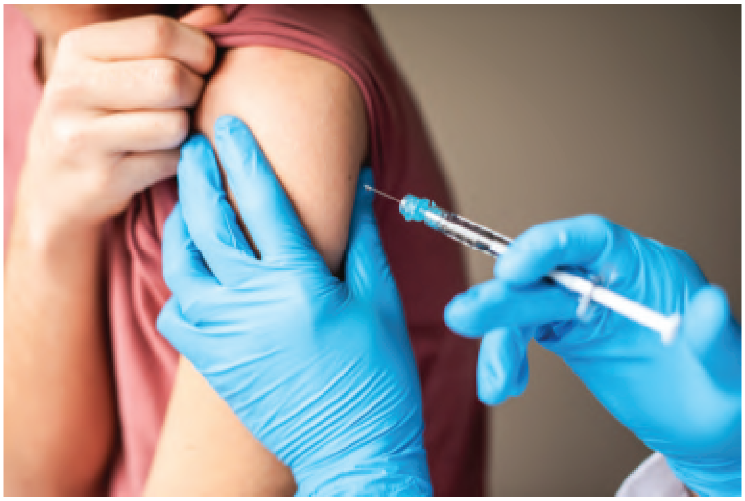

Cavan Images/Shutterstock.com

Figure 9-18 Intramuscular injection. The skin is held taut. The needle is at a 90-degree angle.

The IM route has two advantages over the subcutaneous route:

1. A larger amount of solution can be administered (up to 3 mL, or a maximum of 1 mL in children).
2. Absorption is more rapid because the muscle tissue is more vascular (i.e., contains many blood vessels).

The needle must be long enough to go through the subcutaneous tissue into the muscle. The length of the needle varies with the size of the patient. With a child or very thin, emaciated adult, a 1-inch needle is usually adequate. For most adults, a 1½-inch needle is appropriate. However, for a person with obesity, a 2-inch needle might be required. The needle is inserted at a 90-degree angle with the skin spread taut (Figure 9-18).

Because there are more large blood vessels and nerves in this deeper tissue, the site for injection must be chosen more precisely. Using the illustrations as a guide, follow these steps in selecting the site:

1. ***Ventrogluteal site.*** Can be used for all patients. Position the patient on the back or side (Figure 9-19). Identify the site by placing the palm of your hand on the patient's greater trochanter (use your left hand for the patient's right hip and your right hand for the patient's left hip). Place the index finger on the anterior superior iliac spine and the middle finger on the iliac crest. The injection is made into the center of the V formed between the index and middle fingers.

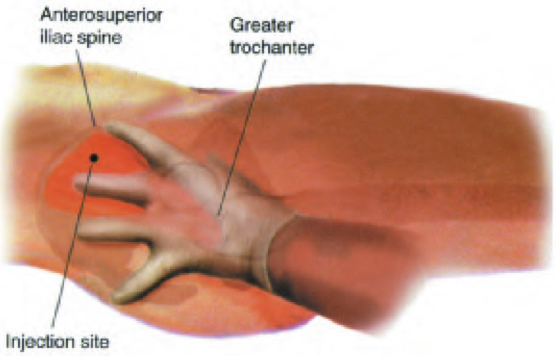


Figure 9-19 Ventrogluteal site for IM injection. Can be administered with patient on back or side.

2. ***Deltoid site.*** The recommended site for vaccines for adults and may be used in children between ages 1 and 18 years for vaccines (Figure 9-20). The maximum solution that can be used is 1 mL; and a shorter needle, 1 inch, is used. Caution must be exercised to avoid the clavicle, humerus, acromion, brachial vein and artery, and radial nerve. Identify the site by drawing a triangle at the midpoint in line with the axilla on the lateral aspect of the upper arm, with the base of the triangle at the acromion process. The injection is made in the center of the triangle.

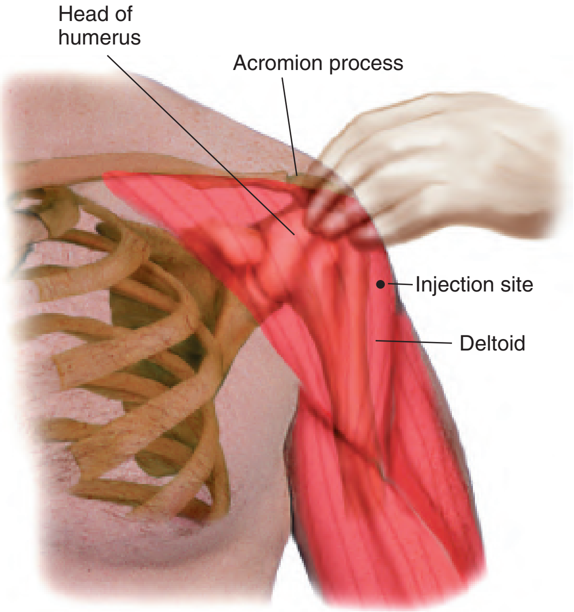


Figure 9-20 Deltoid site for IM injection. Maximum of 1 mL of medication and 1-inch needle is used. Injected above the level of the armpit.

3. ***Vastus lateralis.*** Located on the anterior lateral thigh, the preferred site for infants, since these muscles are the most developed for children under the age of 3 years (Figure 9-21). In the older, nonambulatory, emaciated adult, this muscle may be wasted and insufficient for injection. Identify the site by dividing the thigh into thirds horizontally and vertically, and administer the injection in the middle outer third.

Technique for IM injection is as follows:

1. Wash hands.
2. Assemble the equipment (i.e., correct-size syringe, needle, alcohol wipes, 2 × 2 gauze square, and medication). If an eMAR system is in place, scan the patient and medication.
3. Check the order with the Seven Rights of Medication Administration and draw up the medication, or insert the appropriate prefilled cartridge into the Carpuject holder.
4. After measuring the correct amount of medication in the syringe, draw 0.2 mL of air into the syringe to clear the needle. Recap carefully using the method illustrated in Figure 9-15.

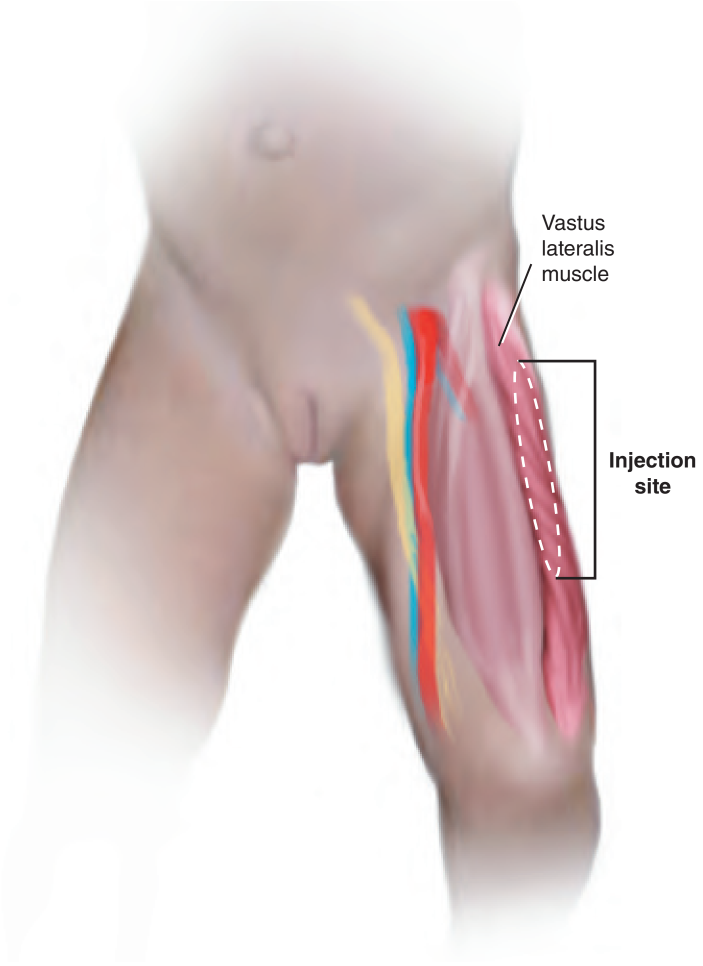


Figure 9-21 Vastus lateralis site for IM injection; preferred for infants. Injected on the anterior lateral thigh.

5. Identify the patient, ask the patient's name and check the armband, and explain the procedure. Use an alternate method to identify the patient if necessary.
6. If the patient is receiving frequent injections, be sure to rotate sites.
7. Put on gloves.
8. Position the patient and expose the area to be used for injection.
9. Cleanse the skin with an alcohol wipe.
10. With your nondominant hand, stretch the skin taut at the injection site.
11. Insert the needle at a 90-degree angle with a quick, dart-like motion of your dominant hand.
12. Inject the medication at a slow, even rate.
13. Withdraw the needle rapidly, holding a dry 2 × 2 gauze pad over the site.
14. Apply pressure and massage the area gently with an alcohol wipe or gauze.
15. Activate the safety device and discard the syringe with needle *uncapped* into the sharps container immediately.
16. Discard gloves and wash hands.

17. Note the medication, dosage, time, date, site of injection, and your signature on the patient's record.
18. Observe the patient for effects and record observations.

The **Z-track method** (Figure 9-22) is recommended for all IM injections, especially those that are irritating to the tissue, such as iron dextran, hydroxyzine, or cefazolin.

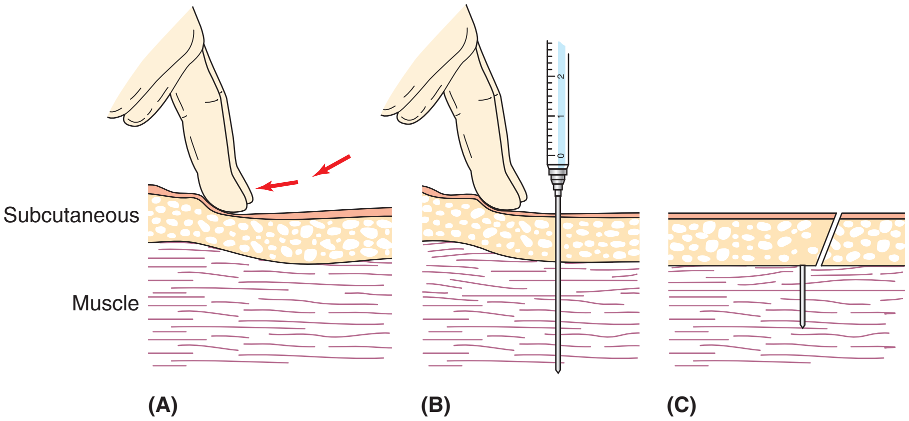


Figure 9-22 Z-track method of IM injection of iron preparations. (A) Skin and subcutaneous tissue pulled to one side and held there. (B) Needle is placed in muscle. (C) Z-track sealed when tissue released.

Technique for the Z-track method is as follows:

1. Draw up the medication and then add 0.3–0.5 mL of air to the syringe. Then replace the needle with a sterile one, 2–3 inches long.
2. Stretch the skin as far as you can to the outer side and hold it there.
3. After cleansing the site, insert the needle with a dart-like motion, and then inject the medication *slowly*. Wait 10 seconds before withdrawing the needle.
4. Withdraw the needle and allow the skin to return to the normal position. This seals off the needle track.
5. Press firmly on injection site with a 2 × 2 gauze square. Do not massage the site because this could spread the medication to the subcutaneous tissue, causing irritation.
6. Advise the patient that walking will aid absorption and to avoid tight-fitting garments that cause pressure on the site.

Clinical Application

One of the main preventions against the COVID-19 virus are the vaccines that have been developed. Vaccines are given IM in the deltoid muscle. It is important to find the anatomical landmarks, clean the site, and use good technique to administer the vaccine.

IV Medications

The IV route involves injecting liquids (medications or fluids) into a vein. The therapeutic effect of this route is immediate. While IV administration may not be within your scope of practice, a familiarity with this route is important. The IV route is used for the following:

- Administer medications
- Correct body fluid imbalances (e.g., dehydration from vomiting)
- Correct electrolyte imbalances (e.g., low potassium)
- Provide some nutritional support to patients who are NPO for a short time
- Administer blood and blood products

There are two types of IV administration: **continuous IV infusion** and **intermittent IV infusion** (*piggyback* or **bolus** or **push**). Both types require similar equipment—an IV catheter inserted in the vein and a bag of IV fluid, a small bag of medication (piggyback), or medication in a syringe.

A physician, registered nurse, or licensed practical nurse is typically responsible for administering IV medications of any type. However, it is important for others on the health care team to understand IV therapy.

Continuous IV infusion

Continuous infusion is administered slowly over long periods of time. The IV solution may or may not contain added medications prescribed by the physician. The bag is hung from an IV pole and typically infused via an infusion pump at a prescribed rate. There are three types of IV solutions classified based on the effect they have on the cell: isotonic (cells remain the same), hypotonic (cells swell), and hypertonic (cells shrink). Table 9-1 lists examples of common IV solutions.

Table 9-1 Types of IV Fluids

Type	Examples and Indications
Isotonic	Normal Saline (NSS or 0.9% NSS) Lactated Ringer's (LR) Whole blood Indicated for fluid replacement
Hypotonic	½ normal saline (½ NS) Dextrose 5% in water (D5W) Indicated to raise total fluid volume, helpful in rehydrating
Hypertonic	Dextrose 5% in 0.9% saline (D5NS) Dextrose 5% in 0.45% saline (D5½NS) Dextrose 5% in lactated Ringer's (D5LR) Indicated for daily maintenance of body fluids, minimal nutrition support and rehydration; hypertonic fluids are most commonly used postoperatively

Intermittent IV Infusion

Piggyback is the term used for medication mixed in an additional bag that contains a small amount (50–100 mL) of IV fluid that is administered over a short period of time at a prescribed interval (e.g., every 4 h). These are most often antibiotics.

Again, an infusion pump is used and set at the prescribed rate. The piggyback is often attached to the main continuous IV infusion.

IV bolus or push is when a medication is not diluted in IV fluid but is injected directly into the IV catheter. It is important that the health care professional administering a bolus or push know the correct rate of administration, because giving a medication too fast could cause serious adverse effects.

Skin Medications

Topical medications for the skin are prescribed for a great variety of conditions and are available in a variety of forms: ointments, lotions, creams, solutions, soaks, and baths. Administration of topical medications requires knowledge of the condition being treated and the purpose of the treatment, and strict adherence to directions as prescribed by the physician or provided by the pharmacist, or to instructions on the medication container or in a package insert. *When in doubt regarding administration techniques, always ask a qualified person for advice*.

Several suggestions for applying topical medications include:

1. For burns, use sterile gloves to apply, and cover with sterile dressings because of the danger of infection. Use a gentle, light touch because of pain.
2. For skin conditions in which there is irritation or itching, use a cottonball or snug-fitting gloves to apply. *Never* use gauze, which can cause additional irritation and discomfort.
3. Follow the physician's order regarding covering or leaving open to the air.
4. Wash old medication off before applying new, unless specifically directed to do otherwise.

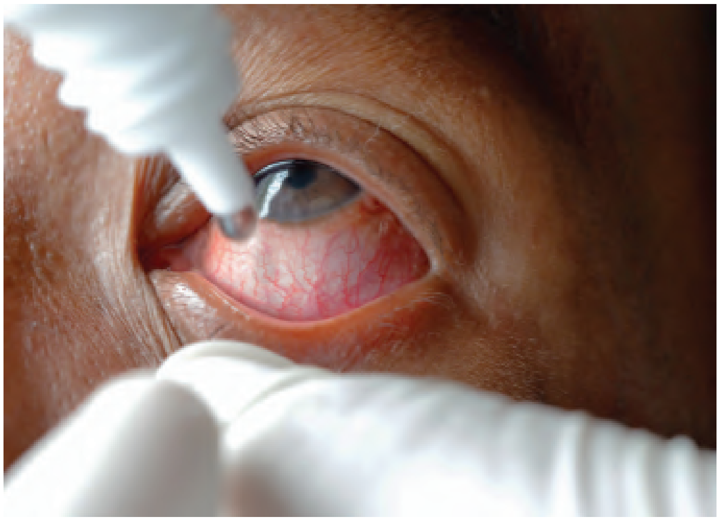
Eye Medications

Technique for instillation of eye medications is as follows:

1. Wash hands.
2. Assemble eye medication (ophthalmic solution or ointment).
3. Check the order with the Seven Rights of Medication Administration. If an eMAR system is in place, scan the patient and medication. Pay particular attention to *percentage* on the medication label and to *which eye* is to be treated (right eye, left eye, or both eyes).
4. Identify the patient, ask the patient's name, and explain the procedure. Use an alternate method to identify the patient if necessary.
5. Put on gloves.
6. Position the patient flat on the back or upright with the head back. Ask the patient to focus eyes upward.
7. Carefully instill the ophthalmic solution, the correct number of drops, or ointment into the lower conjunctival sac, using caution to avoid

contamination of the tip of the dropper or ointment tube (Figure 9-23). Do not let the solution run from one eye to the other.

8. Tell the patient to close the eye gently so as not to squeeze out the solution.
9. Press gently on the inner canthus following administration of eye drops (Figure 9-24). Systemic absorption is thus minimized with medications such as corticosteroids, miotics, and mydriatics.
10. Remove gloves.
11. Wash hands. Replace the medication in an appropriate place.
12. Record the medication, dosage, time, date, and which eye was treated on the patient's record.
13. When more than one eye medication is ordered, wait at least 5 min before instilling the second medication.
14. If eye drops and ointment are ordered for the same time, instill eye drops first, wait 5 min, then apply the ointment.



Anukool Manoton/Shutterstock.com.

Figure 9-23 Instilling eye medication. Gently press the lower lid down and have the patient focus eyes upward. Ophthalmic solution is dropped inside lower eyelid.

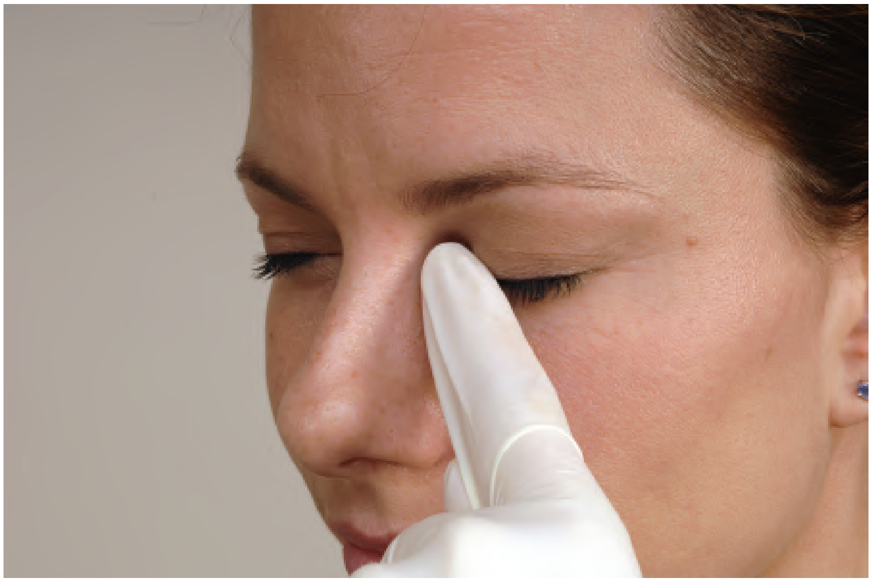
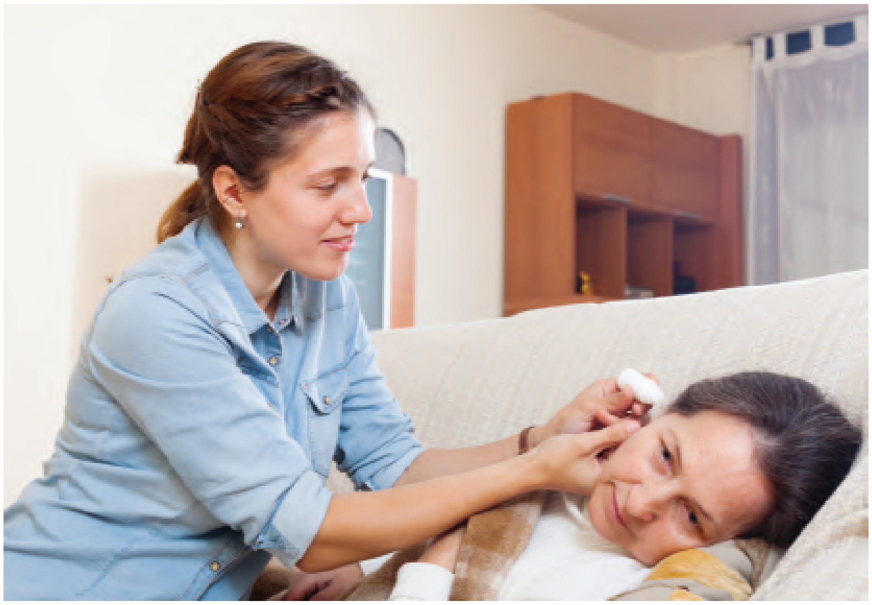


Figure 9-24 Gentle pressure on the inner canthus following administration of ophthalmic medications. Systemic absorption is thus minimized with medications such as corticosteroids, miotics, and mydriatics.

Ear Medications

Technique for instillation of ear medications is as follows:

1. Wash hands.
2. Check the order with the Seven Rights of Medication Administration. If an eMAR system is in place, scan the patient and medication. Pay particular attention to *percentage* on the medication label and to *which ear* is to be treated (right ear, left ear, or both ears).
3. Identify the patient, ask the patient's name, and explain the procedure. Use an alternate method to identify the patient if necessary.
4. Put on gloves.
5. Position the patient lying on their side, or so that their head is tilted to one side, with the desired ear upward (Figure 9-25).
6. Gently shake the bottle; most ear drops are suspensions that need to be shaken. Allow drops to warm in your hands to prevent dizziness and nausea.
7. Grasp just above the earlobe (pinna) and gently pull the ear up and back. For children younger than 3, pull gently down and back.
8. Place the dropper over the ear canal; *Do not* touch the dropper to the ear.
9. Carefully instill the correct number of drops to the ear canal.
10. Press gently on the ear flap and instruct the patient to stay in the sideways position for 1–2 min.
11. Remove gloves.
12. Wash hands. Replace the medication in an appropriate place.
13. Record the medication, dosage, time, date, and which ear was treated on the patient's record.



Iakov Filimonov/Shutterstock.com.

Figure 9-25 Instilling ear drop medication.

When in doubt about administration of any medication, always ask a qualified person for advice. Never guess! Remember that the patient who is receiving the medication could be you or your loved one. By thinking of yourself in the patient's place you will have the proper attitude to administer medications with competence, good judgment, and compassion.

Chapter Review Quiz

Fill in the blanks.

1. Parenteral includes any routes other than the ______________________________

2. Systemic effects are those affecting ______________________________

3. The four parenteral routes with systemic effects include ______________________________

____

____

Label the routes according to their action. Use R for rapid and S for slow. Match each route with the appropriate definition.

	Action (R or S)		Route Definition
4.	______ Sublingual	______	**a.** Given with a needle
5.	______ Transcutaneous	______	**b.** Nebulizer or IPPB
6.	______ Inhalation	______	**c.** Under the tongue
7.	______ Injection	______	**d.** Skin patch

8. What precautions should be observed when applying transcutaneous systems?

____

9. DPI refers to ______________________________

Select the correct needle for the purpose. Needle size may be used for more than one purpose.

	Purpose	Needle
10.	______ Subcutaneous injection	**a.** 21 gauge, 1½ inch
11.	______ Intravenous injection	**b.** 25 gauge, 5/8 inch
12.	______ Allergy testing	**c.** 18 gauge
13.	______ IM injection	**d.** 27 gauge, 3/8 inch

14. What are the two purposes of the tuberculin syringe?

____

____

15. The insulin syringe is calibrated in _______, and 1 mL is equal to _______ in an insulin syringe.

16. On a standard insulin syringe, each calibration represents _______ unit(s).

On a Lo-Dose insulin syringe, each calibration represents _______ unit(s).

Match the injection with the proper technique.

Injection	**Technique**
17. _______ Intramuscular	**a.** Needle 45-degree angle, skin pinched up
18. _______ Subcutaneous	**b.** Needle flat, bevel up, skin taut
19. _______ Intradermal	**c.** Needle 90-degree angle, skin taut

20. List the three sites for IM injections and when each is used.

21. Why is the Z-track method used?

Describe Z-track administration.

22. Define local effects.

List four areas to administer medication for local effects.

23. What are the two types of IV administration?

24. List two examples of IV solutions in each of the categories:

Isotonic solution types

Hypotonic solution types

Hypertonic solution types

25. Which type of needle do you use to withdraw from an ampule?

a. filter

b. 25 gauge

c. non-coring

d. intravenous

26. Which of the following are considered other routes of administration that have mainly local effects? Select all that apply.

a. ear medication

b. eye medication

c. sublingual

d. intramuscular

e. intravenous

Checklist for Intradermal Injection

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked medication order for date, dosage, time, route, and allergies	______	______
3. Identified medication: purpose, side effects, cautions, and normal dosage range	______	______
4. Assembled supplies: TB syringe; 27-gauge, 3/8-inch needle; alcohol wipes; and medication	______	______
5. Checked medication vial against medication sheet using the Seven Rights of Medication Administration; if eMAR system is in place, scanned patient and medication	______	______
6. Withdrew correct dose from vial after cleansing top with alcohol and injecting equivalent amount of air into vial	______	______
7. Recapped needle using sterile technique (refer to Figure 9-15 for technique)	______	______
8. Identified patient by checking bracelet and asking the patient's name and DOB; used an alternate method to identify patient if necessary	______	______
9. Explained procedure to patient and answered any questions regarding procedure	______	______
10. Positioned patient with inner forearm exposed and supported on a flat surface	______	______
11. Put on gloves	______	______
12. Selected area without hair or blemish, cleansed skin with alcohol wipe, and allowed skin to dry	______	______
13. Held patient's arm with nondominant hand, stretching the skin taut	______	______
14. Expelled any air bubbles from syringe	______	______
15. Inserted needle point slowly, bevel side up, only enough to cover needle opening; point of needle visible through skin	______	______
16. Injected medication very slowly, with immediate formation of small bubble	______	______
17. Withdrew needle and applied gentle pressure to injection site with dry gauze (no massage)	______	______
18. Activated the safety device and discarded syringe with needle *uncapped* into sharps container	______	______
19. Removed gloves	______	______
20. Washed hands	______	______
21. Recorded drug name, dosage, time, date, and site of injection on patient's record and signed or initialed entry	______	______
22. Observed patient for 30 min for possible anaphylactic reaction; identified location of emergency equipment and medication if required	______	______
23. Provided written instructions regarding time to return for reading; instructed patient to avoid scrubbing, scratching, or rubbing the area and to report to emergency facility with dyspnea, hives, or rash	______	______

Note: S, satisfactory; U, unsatisfactory.

Checklist for Subcutaneous Injection

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked medication order for date, dosage, time, route, and allergies	______	______
3. Identified medication: purpose, side effects, contraindications, interactions, and normal dosage range	______	______
4. Assembled supplies: 2½- to 3-mL, TB, or insulin syringe; 24- to 26-gauge, 3/8- to 5/8-inch needle; alcohol wipes; and medication vial or ampule	______	______
5. Checked medication against medication sheet using the Seven Rights of Medication Administration; also checked drug for date and discoloration; if eMAR system is in place, scanned patient and medication	______	______
6. Calculated correct dosage on paper if necessary and checked calculations with instructor	______	______
7. If drug is contained in vial, withdrew correct amount after cleansing top with alcohol wipe and injecting equivalent amount of air into vial; if drug is contained in ampule, held tip with alcohol wipe while breaking it at neck; withdrew correct amount of drug without bubbles in syringe; used a filtered needle to administer dose drawn from ampule	______	______
8. Recapped needle using proper sterile technique (refer to Figure 9-15 for technique)	______	______
9. Identified patient by checking identification bracelet and asking the patient's name and DOB; used an alternate method to identify patient if necessary	______	______
10. Explained procedure to patient and answered any questions	______	______
11. Selected appropriate site, using rotation for frequent injections	______	______
12. Put on gloves	______	______
13. Cleansed skin with alcohol wipe	______	______
14. Pinched skin into fold with nondominant hand	______	______
15. Expelled any air bubbles from syringe	______	______
16. Inserted needle at 45- to 90-degree angle and released skin fold	______	______
17. Injected medication slowly	______	______
18. Placed alcohol wipe over entry site and applied pressure as needle was withdrawn	______	______
19. Activated the safety device and discarded syringe and needle *uncapped* in sharps container	______	______
20. Removed and discarded gloves	______	______
21. Washed hands	______	______
22. Recorded drug name, dosage, time, date, site of injection, and signature on patient's record; also recorded effects after appropriate time	______	______

Note: S, satisfactory; U, unsatisfactory.

Checklist for IM Injection

		Rating	
	Activity	**S**	**U**
1.	Washed hands	______	______
2.	Checked medication order for date, dosage, time, route, and allergies	______	______
3.	Identified medication: purpose, side effects, cautions, and normal dosage range	______	______
4.	Assembled supplies: 3-mL syringe; 1½- to 2-inch needle, usually 21-gauge; alcohol wipes; and medication	______	______
5.	Checked medication against medication sheet using the Seven Rights of Medication Administration; if PRN medication, checked time of last dose; if eMAR system in place, scanned patient and medication	______	______
6.	If narcotic, signed and checked time of last dose on controlled substance sheet; calculated correct dosage on paper if necessary and double-checked calculations with instructor	______	______
7.	If drug is contained in *vial*, withdrew correct amount after cleansing top with alcohol wipe and injecting equivalent amount of air into vial; if drug is contained in *ampule*, held tip with alcohol wipe while breaking it at neck; withdrew correct amount of drug without bubbles in syringe; used filtered needle to administer dose drawn from ampule	______	______
8.	*After* measuring the drug accurately in syringe, drew 0.2 mL air into syringe	______	______
9.	Recapped needle using sterile technique (refer to Figure 9-15 for techniques)	______	______
10.	Identified patient by checking bracelet and asking name and DOB; used an alternate method to identify patient if necessary	______	______
11.	Explained procedure to patient and answered any questions	______	______
12.	Closed door to room and/or curtain around bed	______	______
13.	Selected appropriate site, using rotation for frequent injections	______	______
14.	Put on gloves	______	______
15.	Positioned patient appropriately, exposing only the area for injection	______	______
16.	Cleansed skin with alcohol wipe	______	______
17.	With forefinger and thumb of nondominant hand, spread the skin *taut* at injection site	______	______
18.	Inserted needle at a 90-degree angle with a quick, dart-like motion of dominant hand	______	______
19.	Injected medication at a slow, even rate	______	______
20.	Applied pressure with alcohol wipe over entry site as needle was withdrawn rapidly; massaged site gently with gauze unless medication irritating (with cefazolin, hydroxyzine, or iron dextran, pressure only, no massage)	______	______
21.	Made sure there was no bleeding before covering patient and making patient comfortable	______	______
22.	Activated the safety device and discarded syringe and needle *uncapped* in sharps container	______	______
23.	Discarded gloves appropriately; washed hands	______	______
24.	Recorded drug, name, dosage, time, date, site of injection, and signature on patient's record	______	______

Note: S, satisfactory; U, unsatisfactory.

Checklist for Instillation of Eye Medication

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked the order with the Seven Rights of Medication Administration; noted percent of strength of drug, which eye, and allergies; if eMAR system is in place, scanned patient and medication	______	______
3. Identified medication: purpose, side effects, and cautions	______	______
4. Identified patient by checking bracelet and asking the patient's name and DOB; used an alternate method to identify patient if necessary	______	______
5. Explained procedure to patient and answered any questions regarding procedure	______	______
6. Positioned patient on back or upright with head back	______	______
7. Asked the patient to focus eyes upward	______	______
8. Used aseptic technique to instill correct number of drops or ointment dosage into lower conjunctival sac	______	______
9. Gently closed the eyelid and applied pressure to the inner canthus (eye drops only)	______	______
10. Washed hands and replaced medication in appropriate place	______	______
11. Recorded medication, dosage, time, date, and which eye was treated on patient's record	______	______

Note: S, satisfactory; U, unsatisfactory.

Procedural note: If more than one eye medication is ordered, wait at least 5 min before instilling the second medication. If eye drops and ointment are ordered for the same time, instill eye drops first, wait 5 min, and then apply the ointment.

Checklist for Instillation of Ear Medication

	Rating	
Activity	**S**	**U**
1. Washed hands	______	______
2. Checked the order with the Seven Rights of Medication Administration; noted percent of strength of drug, which ear, and allergies; if eMAR system is in place, scanned patient and medication	______	______
3. Identified medication: purpose, side effects, and cautions	______	______
4. Identified patient by checking bracelet and asking the patient's name and DOB; used an alternate method to identify patient if necessary	______	______
5. Explained procedure to patient and answered any questions regarding procedure	______	______
6. Positioned patient on side or with head tilted sideways	______	______
7. Pulled the pinna in the correct direction based on patient age	______	______
8. Used aseptic technique to instill correct number of drops	______	______
9. Gently pressed on the ear flap and ensured the patient remained sideways for 1–2 min	______	______
10. Washed hands and replaced medication in appropriate place	______	______
11. Recorded medication, dosage, time, date, and which ear was treated, on patient's record	______	______

Note: S, satisfactory; U, unsatisfactory.

Chapter 10

Poison Control

Key Terms and Concepts

Antidotes

Antivenom injections

Emetic

Ingestion

Poison

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify four routes by which poisons may be taken into the body.
2. List five conditions in which vomiting after the ingestion of poisons could be injurious to the patient.
3. Describe the first step to take in the event of any poisoning and the procedure to follow.
4. Explain the purpose of activated charcoal and when it is given.
5. Describe clinical procedures required when caring for patients who have been poisoned.
6. Describe appropriate therapy for poisoning by inhalation, external poison, and insect sting.
7. Identify two groups of people at risk for poisoning.
8. List 10 recommendations for patient education to help prevent poisoning.

A **poison** is a substance which, when taken into the body by ingestion, inhalation, injection, or absorption, interferes with normal physiological functions. In some cases, only a small amount of a substance can cause severe tissue damage directly (e.g., corrosives such as acids). In other cases, the substance can be beneficial in small amounts but lethal in excessive amounts (e.g., overdose of medication).

In a case of suspected poisoning, the best policy is to contact a Poison Control Center directly or through an emergency care facility. Instructions can then be given by phone for appropriate emergency treatment based on the type of poison and the patient's condition, age, and size.

Poisoning by Ingestion

The most common type of poisoning is by **ingestion** or swallowing. Children between the ages of 1 and 5 are most at risk for poisoning. Before 2004 it was recommended that children who had ingested poisons be given the **emetic** ipecac syrup to induce vomiting. However, extensive research conducted through the American Association of Poison Control Centers, Toxic Exposure Surveillance System, identified several concerns regarding ipecac, which are as follows:

1. Outcomes failed to justify its effectiveness.
2. Adverse effects, such as persistent vomiting, could interfere with other treatment.
3. There has been evidence of widespread abuse of ipecac by people with anorexia and bulimia.

Therefore, in early 2004, the American Academy of Pediatrics (AAP) issued a policy statement on poison treatment in the home. The AAP recommended against keeping ipecac in the home and further recommended that ipecac presently in the home be disposed of safely.

The first step to take in any poisoning is to contact your local Poison Control Center. This number can be obtained by calling the national toll-free Poison Control number: **1-800-222-1222**. This number should be programmed into your phone for quick access in time of emergency. Callers should be prepared to give details regarding the poison as well as the age, weight, and health status of the individual who took the poison. Mention allergies and asthma if present.

Under the following conditions, vomiting could be injurious to the patient and should be avoided if possible:

1. Ingestion of corrosive substances such as mineral acids or caustic alkalis (e.g., carbolic acid, ammonia, drain cleaners, oven cleaners, dishwasher detergent, and lye). Check also for burns around or in the mouth. If the ingested substance burned tissue on the "way down," it is likely it will also burn and damage tissue on the "way back up" and therefore vomiting can cause additional tissue damage.

Clinical Connection

Poison Control Center versus 911 Emergency Services

Poison Control Centers are the best resource for finding out information about the exposure to poisons and other harmful substances and what to do in these situations. That being said, patients should be properly educated that this should not be the first phone call in a medical emergency. If a person is unconscious and/or has severe changes in vital signs, cognition, or behavior after ingesting a substance, the quickest way to get them help is to call 911. Additionally, this is especially important if you are not absolutely certain what substance was ingested, which is often the case when a person is found unconscious. In a medical emergency, after calling 911 it is then okay to call a Poison Control Center to get more information. Educating patients to make this distinction could be the difference between saving a life and permanent damage or death.

2. Ingestion of volatile petroleum products (e.g., gasoline, kerosene, lighter fluid, and benzene). Vomiting can cause aspiration and/or asphyxiation (suffocation).
3. Ingestion of convulsants (e.g., strychnine or iodine). Vomiting can precipitate seizures.
4. If the patient is semiconscious, is severely inebriated, is in shock, is convulsing, or has no gag reflex, vomiting could cause choking, aspiration, and/or asphyxiation.
5. If the patient is less than 1 year old.
6. In patients with cardiac or vascular disease, vomiting can increase blood pressure and precipitate a stroke, cardiac arrhythmias, or an atrioventricular block.

If any of these conditions exist, the patient should be transported *immediately* to an emergency care facility. Trained personnel can remove the stomach contents by gastric lavage, if appropriate, and administer appropriate antidotes as indicated.

Antidotes, such as flumazenil or naloxone and/or CPR (cardiopulmonary resuscitation), may be required in poisoning with central nervous system depressants. The routine use of gastric lavage is no longer recommended by the American Academy of Clinical Toxicology and, because of the danger of perforating the damaged tissue of the esophagus, is *not* used in patients who have ingested corrosives. If perforation exists, surgery is required. Observation is required in an acute care facility.

Sometimes a substance such as activated charcoal is administered by mouth to minimize systemic absorption of the ingested poison. If indicated, gastric lavage followed by, or preceded and followed by, activated charcoal may be more effective than activated charcoal alone. However, if activated charcoal is given, it may interfere with antidotes given via the gastric route as well (e.g., *n*-acetylcysteine for Tylenol poisoning), but the clinical significance of this is unknown.

Personnel caring for poisoning victims should observe the following cautions:

- *Be sure to save emesis*. It may be necessary to send it to a laboratory to determine the type of poison. In addition, save any evidence of what may have caused the poisoning such as plant parts, mushrooms, pills, and so on. If there is doubt about the poison, the physician may also order urine and blood tests for toxicology.
- Closely monitor the vital signs of patients who have taken poison of any kind.
- Observe closely for possible confusion, tremors, convulsions, visual disturbances, loss of consciousness, respiratory distress, or cardiac arrhythmias.

Poisoning by Inhalation

Poisoning by inhalation requires symptomatic treatment: fresh air, oxygen, and CPR if indicated. Incomplete combustion and fires can produce carbon monoxide. Carbon monoxide poisoning can quickly rob the tissues of vital oxygen, and high-percentage oxygen therapy or even oxygen under pressure (hyperbaric oxygen) in severe cases may be needed. Inhaling insect spray may require administration of an antidote such as atropine.

External Poisoning of Skin or Eyes

External poisons should be flushed from the skin for 20 min and from the eyes for 30 min with a continuous stream of water. The patient should then be transported to an emergency care facility for further treatment as required. Systemic absorption of poisons through the skin may require administration of an antidote.

Poisoning by Sting and Snakebite

Poisoning by an insect injecting venom by sting (e.g., bee, wasp, scorpion, or fire ant) should be treated by cleansing the area, immediately removing the stinger, and applying an icepack to the site of the sting. If the patient is allergic, watch closely for possible anaphylactic reaction. CPR and administration of epinephrine and corticosteroids may be required. Transport the patient to an emergency care facility immediately if indicated. Some persons with allergies carry a kit with medication prescribed by their physician (e.g., an epinephrine auto-injector for self-injection or injection by someone else).

Anton_Ivanov/Shutterstock.com.

After emergency care is completed, aftercare to lessen the pain, discomfort, and redness associated with stings can include application of topical corticosteroid ointment.

Do not apply ice or apply a tourniquet to a snakebite. Venom is very irritating and may cause sloughing of the tissues. Keep the patient quiet to slow circulation, and transport the patient, lying down, to an emergency care facility for **antivenom injections**. If possible, take the snake along, in a closed container, for identification purposes. It may be nonpoisonous.

Patient Education

Patients with known allergies should be instructed on the following:

1. Be particularly careful when working outdoors and do not approach any insect nests or hives. Have lawn areas and shrubbery periodically inspected for insect nests and colonies.
2. Always wear shoes and light-colored clothing when outside. If possible, wear long sleeves and pant legs.
3. Remove the stinger by scraping it off with the edge of something rigid such as a credit card. Pulling a stinger out with tweezers may actually cause more poison to be injected into the body as you squeeze the stinger.
4. If epinephrine or a self-injected device is prescribed, the patient should be instructed on its use.

People at Risk

Poisonings are the leading cause of health emergencies for children across the nation and a major cause of death among young children because of their natural curiosity and active lifestyle. The danger is particularly great with flavored medications, such as aspirin and iron tablets. Great care must be taken to prevent poisoning of young children. Children between the ages of 1 and 5 years are most at risk.

Keep all chemicals in a locked cupboard. Keep infrequently used drugs, for example, pain medications, in a lockable box such as a tackle box or file box. Be sure that medications taken daily by adults are always in childproof containers. Be particularly vigilant when visiting with older adult friends or relatives who may not have childproof containers for their pills. Be aware that the most common sources for poisoning in children under age 6 are cosmetics and personal care products.

The health care professional can play a major role in reducing the number of accidental poisonings in children by stressing preventive measures to parents and caregivers. Participation in community-based education programs and school workshops can help spread the word on poisonings and increase awareness.

Sometimes, when a person is prescribed antibiotics, they do not finish the entire supply of medication (even though they are directed to do so). This opens the opportunity for the drug to expire in the person’s medicine cabinet. The next time the person is ill, they may be tempted to take these expired antibiotics. Any expired drug has the potential to become a poison, as some drugs break down after their expiration date into toxic byproducts. Even if a drug is not poisonous, antibiotics will likely be less effective due to a decrease in strength. Certain expired medications are at risk of bacterial growth and sub-potent antibiotics can fail to treat infections, leading to more serious illnesses and antibiotic resistance.

Another group at risk for poisoning is older adults. Overdoses of medication can result in toxicity, with symptoms of confusion, dizziness, weakness, lethargy, ataxia, tremors, or cardiac irregularities. Toxic reactions from medications taken by older adults can possibly result from the following:

1. Slower metabolism, impaired circulation, and decreased excretion causing medication to remain in the body longer and build up to dangerous levels
2. Wrong dosage caused by patients with low vision or poor memory (patients may forget that they have taken medicine and take a double dose)
3. Interactions when many different medications are taken and over-the-counter medications or herbal remedies are self-administered with inadequate medical supervision
4. Medical conditions affecting absorption

Many medicines and common household products resemble candy or food. Children may be attracted to the unique shapes and bright colors used in packaging. Low vision may contribute to mistakes by adults, especially older adults. It is important to keep medicines and dangerous chemicals in an area separate from food and medicines. Don't be confused by look-alikes (Figure 10-1).

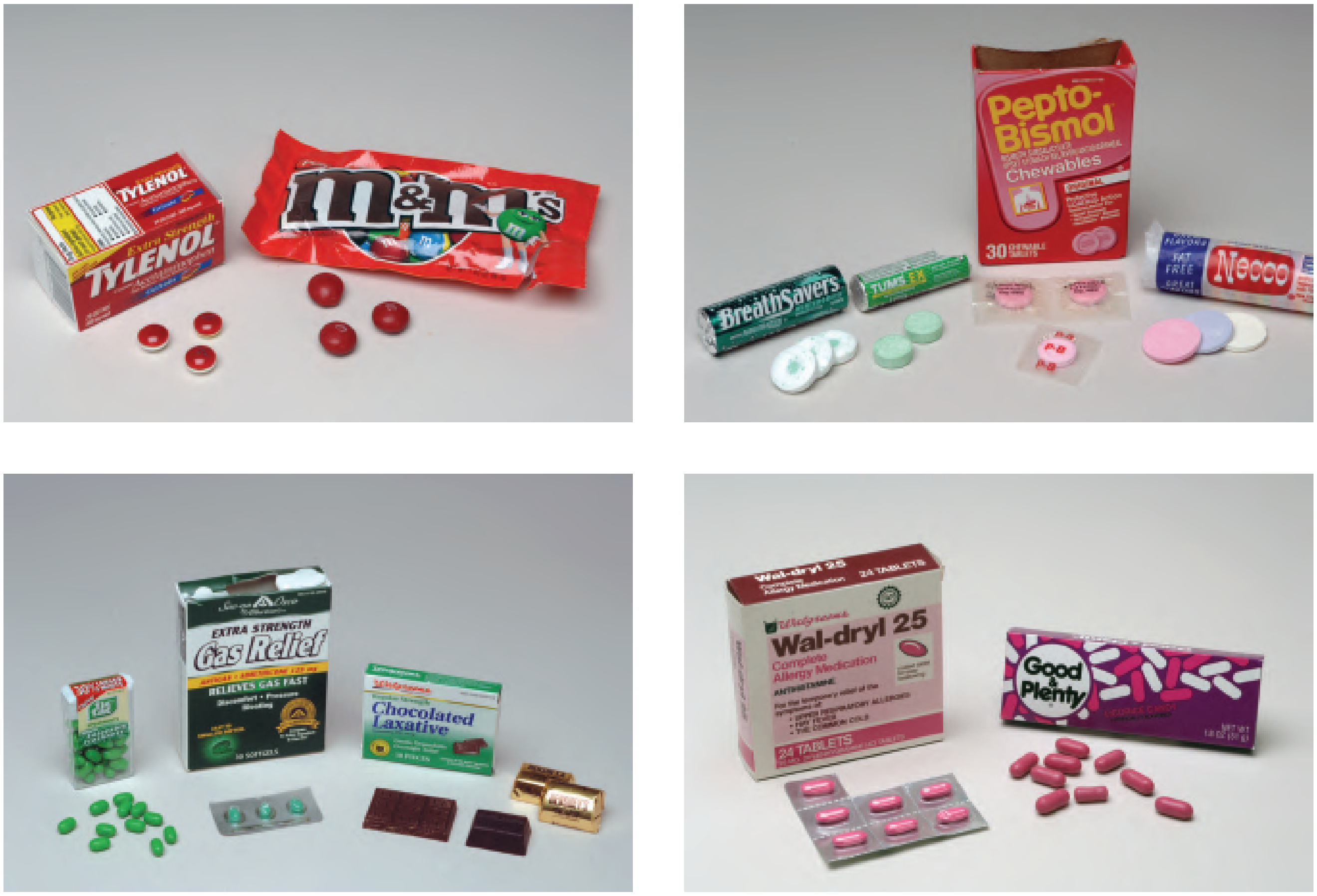


Figure 10-1 Look-alikes: Don't be confused! The photos show side-by-side comparisons of a medicine along with a potential look-alike candy. Keep these products in separate areas. (**Note:** The compared products are chosen for illustration purposes only. The manufacturers do not intend any misuse of their products.)

Patient Education

Poisons

Public education is most important in preventing poisoning. The public must be instructed in precautions with medications, and it is especially important to inform the parents and caregivers of young children and older adults. It is the responsibility of all health care professionals to provide the necessary information to help prevent poisoning.

To prevent poisoning, the American Medical Association recommends the following precautions:

1. Keep all medicines, household chemicals, personal care products, cleaning supplies, and pesticides in a locked cupboard. There is no place that is "out of reach of children."
2. Never transfer poisonous substances to unlabeled containers or to food containers such as milk or soda bottles or cereal boxes. Keep in the original labeled container.
3. Never store poisonous substances in the same area with food. Confusion could be fatal.
4. Never reuse containers of chemical products.
5. Do not give or take medications in the dark.
6. Never leave medications on a bedside stand. Confusion while a person is sleepy could result in a fatal overdose.
7. Always read the label before taking any medication or pouring any solution for ingestion.
8. Never tell children the medicine you are giving them is candy. Explain to children that medication is taken for your well-being and that all medication is to be taken only as directed by a physician.
9. When preparing a baby's formula, taste the ingredients. Never store boric acid, salt, or talcum near the formula ingredients.
10. Never give or take any medication that is discolored, has a strange odor, or is outdated.
11. Do not take medicine in front of children.
12. Keep pocketbooks, purses, and pillboxes out of reach of children. Do not allow children access to cosmetic products.
13. Rinse out containers thoroughly before disposing of them.

Note: In the past, most people flushed old medicines down the toilet to prevent accidental poisonings of children and animals who may find medicines in the trash. Drugs such as powerful narcotic pain relievers and other controlled substances carry instructions for flushing to reduce the danger of unintentional use or overdose and illegal abuse.

Despite the safety reasons for flushing drugs, some people are questioning this practice because of concerns about trace levels of drug residues found in surface water, such as rivers and lakes, and in some community drinking water supplies. However, the main way drug residues enter water systems is by people taking medications and then naturally passing them through their bodies.

To address this concern, the Food and Drug Administration (FDA) recommends mixing most medicines with kitty litter or used coffee grounds, placing the mixture in a sealed container or plastic bag, and disposing of it in your household trash. Pharmacies often have kiosks available for disposal of medications, with the exception of controlled substances. In addition, many cities and towns have medicine take-back programs or household hazardous waste facilities where you can bring your old medicines. When in doubt, ask your pharmacist about proper disposal in your area. The FDA's recommendations regarding disposal of unused medicines can be found at their website.

Obtain the number of your nearest Poison Control Center and place it on or near your telephone; also program it into your cell phone. There are more than 72 Poison Control Centers throughout the United States and Canada with computerized data to give you the latest information about poisons. Remember, *the wrong treatment is often more dangerous than no treatment*. You can obtain the number of the Poison Control Center in your area of the United States by calling 1-800-222-1222 or the nearest emergency care facility, by logging on to the website (http://www.aapcc.org) of the American Association of Poison Control Centers, or by checking the emergency numbers in your phone book or online. Canada does *not* have a national Poison Control Center number. Obtain the number of your nearest Poison Control Center in Canada by logging on to the website (http://www.capcc.ca) of the Canadian Association of Poison Control Centers. The Poison Control Center is also a good source of information regarding poisonous plants, insects, snakes, reptiles, and poisonous marine organisms such as stingrays and jellyfish.

Chapter Review Quiz

Complete the statements by filling in the blanks.

1. Poisons can be taken into the body in four different ways:

2. In cases of poison ingestion, vomiting is to be avoided under the following five conditions:

3. Gastric lavage is contraindicated when a patient has ingested what type of substance?

4. When is activated charcoal administered?

5. Why are gastric contents saved after emesis or gastric lavage?

6. What is the treatment for poisons that contact skin or eyes?

7. What two groups of people are most at risk for poisoning?

8. Name four conditions that may lead to toxic medication reactions in older adults.

9. What is the leading cause of poisoning deaths in children under 6 years of age?

10. What is the number of the National Poison Control Center?

11. In what scenarios is it appropriate to call 911 before poison control?

12. What is the procedure for poisoning of eyes and skin?

13. List 10 recommendations for patient education to prevent poisonings.

Note

A Comprehensive Review Exam for Part I can be found at the end of the text following the Summary.
Answers to this comprehensive exam are available from your instructor.

PART 2

Drug Classifications

Chapter 11

Nutritional Concepts of Pharmacology

Key Terms and Concepts

Antioxidants
Deficiency
Dietary Reference Intakes (DRIs)
Electrolytes
Fat-soluble vitamins
Herbal
Hyperkalemia
Minerals
Overdoses
Supplements
Symptoms of overdose
Toxicity
U.S. Recommended Dietary Allowances (U.S. RDAs)
Water-soluble vitamins

Objectives

Upon completion of this chapter, the learner should be able to:

1. Categorize vitamins as water-soluble or fat-soluble.
2. List vitamins and their sources, functions, signs of deficiency, and symptoms of overdose if known.
3. Describe common electrolytes and their normal blood chemistry values.
4. Identify vitamins by name and letter.
5. List minerals and their sources, functions, and signs of deficiency.
6. Identify the chemical symbol for each mineral.
7. Describe medical conditions that may require vitamin or mineral supplements.
8. Explain the role of antioxidants in nutrition therapy.
9. Describe why and how consumers should be more vigilant in the use of herbal products.

Dietary requirements for vitamins and other nutrients may be listed in several ways:

U.S. Recommended Dietary Allowances (U.S. RDAs) gives vitamins and minerals necessary for the maintenance of good nutrition in the average healthy adult under typical living conditions in the United States. The Food and Drug Administration (FDA) uses RDAs to develop daily values (seen on most product labels) to help consumers compare the nutrient content of products.

Adequate intake (AI) is based on observed or experimentally determined estimates of nutrient intake by healthy people and used when data to calculate an RDA are insufficient.

Tolerable upper intake level (UL) is the highest level of daily consumption that current data have shown to cause no side effects when used indefinitely without medical supervision.

Dietary Reference Intakes (DRIs) are a system of nutrition recommendations from the Institutes of Medicine of the U.S. National Academy of Sciences. These recommendations consist of the RDAs, AIs, and ULs listed here.

Under special circumstances, vitamin and mineral **supplements** are required for a person's optimal function and health. *Indications for vitamin and mineral supplements include the following*:

Inadequate diet. Because of anorexia, weight reduction, or other special diets, illness, alcohol use disorder, or poor eating habits

Malabsorption syndromes. Chronic gastrointestinal (GI) disorders or surgery that results in chronic diarrhea

Increased need for certain nutrients. As in pregnancy and lactation (especially iron, folic acid, and calcium), infants under one year of age, adolescents, older adults, debilitation, illness, unusual physical activity, and postmenopausal females (calcium)

Deficiency due to medication interactions. For example, potassium deficiency with the use of diuretics

Nutrients function in groups or teams. Therefore, if diet supplementation is warranted, it is likely that both vitamins and some additional minerals are needed. An example of this teamwork is bone growth, development, and strength, which depend on calcium, magnesium, vitamin A, vitamin D, and several other nutrients (fluoride, etc.). However, patients should be advised to avoid self-medication with large doses of vitamins or minerals, which may not be indicated if the diet is well balanced and the individual is in good health. **Overdoses** of some vitamins, especially A and D, and some minerals, for example, iron, can be injurious to health. A need or **deficiency** should be established by a physician's diagnosis or blood test before exceeding the RDA. Supplementary (prophylactic) multivitamin preparations may reasonably contain 50%–150% of the RDA of vitamins (except the amount of vitamins A and D and folic acid should not exceed the RDA). Combination vitamin preparations containing iron should not be used unless a deficiency has been established with a blood test or physician's diagnosis.

It is important to differentiate between water-soluble and fat-soluble vitamins to avoid their build-up in the body with possible **symptoms of overdose**. Megadoses of vitamins (more than the RDA) should be taken only if prescribed by a physician and/or approved by the FDA. *Remember, the RDA includes the amount of vitamins from foods you eat as well as supplements.* Research reports have indicated a possibility of damage to tissues with large quantities of vitamins (above the RDA), especially those stored in the fat cells of the body.

The RDAs and DRIs listed on the following pages are established for average, healthy adults. Larger amounts are required with certain conditions (e.g., pregnancy, lactation, and some illnesses). Larger amounts are required for males than females. Smaller amounts are required for children (consult references). However, megadoses should *never* be taken except under the direct supervision of a physician.

The RDA and DRI are presented here only for reference. You are not expected to remember these figures. However, before taking any supplements or educating patients on supplements, it is wise to consult references for appropriate doses and to avoid overdosage. Overdosage can sometimes cause severe adverse effects and even acute **toxicity**, especially with the fat-soluble vitamins.

Fat-Soluble Vitamins

The **fat-soluble vitamins** are vitamins A, D, E, and K.

Vitamin A (Retinol, Retinal, Beta Carotene)

Vitamin A is processed in the body from the carotene of plants, especially yellow-orange and dark-green leafy vegetables, fruits, oily saltwater fish, dairy products, and eggs (RDA: 800–1,000 units per day, DRI: 700–3,000 mcg per day). Beta carotene is an antioxidant (review the “Antioxidants” section later in this chapter).

Necessary for:

Resistance to infection
Proper visual function at night
Normal growth and development of bones and soft tissues, and maintenance of healthy epithelial tissues (skin and mucous membranes)
Healing of wounds (sometimes prescribed for acne)
Reproduction

Deficiencies may result from:

Malabsorption of fats
Diarrhea
Obstruction of bile

Signs of deficiency include:

Night blindness
Slow growth, anorexia, weight loss, bone and teeth deformities
Dry eyes and skin, pruritus (itching)

Supplements of vitamin A (e.g., Aquasol A) may be necessary for:

Infants fed unfortified skim milk or milk-substitute formulas
Those with prolonged infection or fever
Those with diabetes or hypothyroidism
Those with liver disease
Vitamin A has been used as a screening test for fat absorption.

Some dermatological disorders are treated with retinoids (synthetic vitamin A products). One retinoid product, isotretinoin, is prescribed for severe acne; another is acitretan, used for severe psoriasis. Retinoids can cause fetal abnormalities and are therefore contraindicated in pregnancy. They have also caused increased intracranial pressure, possible liver injury, and other adverse side effects associated with hypervitaminosis A. Note that vitamin A deficiency is the leading cause of blindness in children worldwide.

Symptoms of overdose (hypervitaminosis A) from greater than 50,000 units (15,000 mcg of retinol) in adults and 2,000 units (6,000 mcg of retinol in infants and children) include:

❗ Irritability, psychiatric symptoms
Fatigue, lethargy
Headache, insomnia
❗ Brittle nails, dry skin, and dry hair
❗ Anorexia, nausea, diarrhea, jaundice
Acute toxicity with increased intracranial pressure, vertigo, coma
❗ Joint pain, myalgia
Stunted growth, fetal malformations

Caution should be used with kidney or liver problems or diabetes.

❗ Long-term use of large doses of vitamin A is *contraindicated* for females who are, or may become, pregnant. *Fetal malformations* have been reported following maternal ingestion of large doses of vitamin A, either before or during pregnancy. Many medications that are vitamin A derivatives, such as tretinoin cream, are also contraindicated during pregnancy.

Vitamin D (D_2-Calciferol, D_3-Cholecalciferol, D_2-Ergocalciferol)

Vitamin D is synthesized in the body through the action of sunlight on the skin. Other sources include fish oils (especially salmon, tuna, and mackerel) and food products fortified with vitamin D, such as milk and cereals (RDA: 400 units per day, DRI: 5–15 mcg per day). Vitamin D_3 is the form seen in products containing 10,000 units or less of vitamin D; D_2 is the form seen in products containing 50,000 units of vitamin D. Cholecalciferol or D_3 is more effective in raising vitamin D serum concentrations.

Earlier research studies have shown that people with low vitamin D levels are twice as likely to develop coronary artery disease, heart failure, stroke, high blood pressure, and diabetes as those with normal levels. Vitamin D deficiency is common in the northern latitudes, where people do not get much sunlight and spend much of their time indoors.

The National Institutes of Health (NIH) has compiled a list of individuals who need increased vitamin D, and these include:

- Breastfed infants
- People who are 50 years or older
- Those with limited sun exposure
- Dark-skinned people
- People with obesity (BMI greater than 30)

Consequently, several researchers have suggested that the use of vitamin D supplements be increased; however, the risk of overdose and toxicity must be considered. Vitamin D is fat-soluble, stays in the system longer, and can accumulate to toxic levels. Those taking large doses must be assessed carefully for symptoms of toxicity, which are listed shortly.

Necessary for:

- Maintenance of normal nerves and muscles
- Regulating the absorption and metabolism of calcium and phosphorus for healthy bones and teeth
- Pregnancy and lactation, when it is especially important

Signs of deficiency include:

- Poor tooth and bone structure (rickets)
- Skeletal deformities
- Osteoporosis, osteomalacia
- Tetany (muscle spasms)

Vitamin D supplements are prescribed as calcitriol (Rocaltrol) or ergocalciferol (Drisdol) to prevent or treat rickets or osteomalacia and to manage hypocalcemia in cases of renal disease or parathyroid malfunction. The difference between the therapeutic dosage and that causing hypercalcemia is very small; therefore, dosage must be carefully regulated and monitored.

Symptoms of vitamin D overdose and toxicity include:

- ❗ Nausea, anorexia, weight loss
- ❗ Muscle and/or bone pain
- ❗ Kidney damage and kidney stone formation
- ❗ Heart rhythm abnormalities
- ❗ Hypercalcemia with convulsions or confusion
- ❗ Fetal disorders

Caution not to exceed the RDA of vitamin D, especially with:

- Cardiovascular disorders
- Kidney diseases
- Pregnancy (possible fetal malformations or intellectual disabilities)
- Lactation

Interactions may occur (overdose may antagonize) with:

- Digoxin
- Mineral oil may interfere with intestinal absorption of vitamin D.

Vitamin E (Tocopherol)

Vitamin E is abundant in nature and is found especially in cereals, wheat germ, seeds, nuts, vegetable oils, eggs, meat, and poultry (RDA: 30 units per day, DRI: 15–1,000 mg per day). Vitamin E has antioxidant properties (refer to the “Antioxidants” section later in this chapter).

Necessary for:

Normal metabolism

Protection of tissues of the eyes, skin, liver, breasts, muscles, and lungs

Protecting red blood cells (RBCs) from damage

Decreasing platelet clumping

Off-label uses include vitamin E supplements as one of the treatment protocols for management of early Alzheimer's disease and for possibly slowing the progress of such symptoms as memory loss. However, such supplements will neither cure nor prevent the disease.

Note

In general, vitamin E supplements should be taken at the lowest dosage necessary; this is especially true while on anticoagulant therapy because of increased risk of bleeding (including cerebral hemorrhage).

Deficiencies are found in those with:

Alcohol abuse

Malabsorption syndromes, for example, celiac disease, sprue, cystic fibrosis

Pathological conditions of the liver and pancreas

Sickle-cell anemia

Also found in premature infants or low-birth-weight neonates

Signs of deficiency are not firmly established. Premature infants may show irritability, edema, or hemolytic anemia. Adults who are vitamin E deficient may show muscle weakness and some abnormal laboratory values, such as low red blood cell (RBC) count.

! **Vitamin E overdose** (1,200 units) can result in bleeding in patients who are vitamin K deficient or on oral anticoagulants.

Interactions: Excessive use of mineral oil may decrease the absorption of vitamin E.

Vitamin K (Phytonadione)

Vitamin K is found in green and leafy vegetables, cabbage, vegetable oils, cheese, eggs, and liver, and is absorbed in the small intestine in the presence of bile salts (RDA: 60–80 mg per day, DRI: 90–120 mcg per day).

Necessary for blood clotting. Unlike other fat-soluble vitamins, the body does not store vitamin K, but recycles it in less significant amounts.

Deficiencies may result in low blood clotting factor levels caused by:

Insufficient vitamin K stores in the newborn

Inadequate dietary intake

Malabsorption syndromes, ulcerative colitis, prolonged diarrhea

Warfarin overdose

Prolonged use of salicylates, quinine, long-term parenteral nutrition, and broad-spectrum antibiotics

Signs of deficiency include:

Increased clotting time

Petechiae and bruising

Blood in the urine (hematuria) or stool (melena or hematochezia)

Vitamin K is usually administered orally or intravenously. Injectable vitamin K package inserts warn against intravenous (IV) administration due to the possibility of severe allergic reactions. However, IV administration is recommended as the route of choice by the American College of Chest Physicians for serious bleeding related to vitamin K deficiency or as an antidote for bleeding complications during warfarin therapy. Vitamin K is effective only for bleeding disorders caused by low concentrations of vitamin K–dependent blood clotting factors. It is not effective for bleeding from other causes such as heparin overdose or the newer oral anticoagulants.

The American Academy of Pediatrics recommends that vitamin K (phytonadione) be routinely administered to infants at birth to prevent hemorrhagic disease of the newborn. Some state regulations currently require this prophylaxis.

Adverse effects are rare, but hypersensitivity reactions have occurred with IV injections. Toxicity in infants can cause jaundice or hemolytic anemia.

Note

Patients receiving anticoagulant therapy should be consistent in the amount of vitamin K–rich foods, such as green leafy vegetables, they eat daily to keep the levels of prothrombin and other vitamin K–dependent clotting factors stable. Large amounts of vitamin K–rich foods can counteract anticoagulant therapy.

Clinical Application

Warfarin and Vitamin K

Currently, warfarin is one of the oldest anticoagulants used. It was assumed that as newer medications (Pradaxa and Xarelto) came onto the market, warfarin would be used less and become obsolete due to its interactions with food and its variable effectiveness. It turns out that this is not the case, and warfarin is still used as a primary anticoagulation treatment. This is because it is much cheaper than newer options and has a readily available antidote (vitamin K), which is a major advantage over other anticoagulants when serious bleeding occurs.

Water-Soluble Vitamins

The **water-soluble vitamins** include the B-complex vitamins and vitamin C.

Vitamin B_1 (Thiamine)

Vitamin B_1 is a coenzyme utilized in carbohydrate metabolism. It is found in whole grains; wheat germ; peas; beans; nuts; yeast; meat, especially pork and organ meats; oysters; collard greens; oranges; and enriched cereals (DRI: 1.1–1.4 mg per day).

Necessary for normal function of the nervous and cardiovascular systems.

Deficiencies in the United States may be due to:

Alcohol use disorder and substance abuse
Malabsorption and liver disease

Signs of deficiency (beriberi; symptoms are sometimes vague) include:

Anorexia and constipation, GI upset, nausea
Neuritis, pain, tingling in extremities, loss of reflexes
Muscle weakness, fatigue, ataxia

Mental depression, memory loss, confusion

Cardiovascular problems

Hypersensitivity reactions have occurred mainly following repeated IV administration of the drug.

Vitamin B_2 (Riboflavin)

Vitamin B_2 is a coenzyme utilized in the metabolism of glucose, fats, and amino acids. It is found in milk; eggs; nuts; meats, especially liver; yeast; enriched bread; and green leafy vegetables (DRI: 1.3–1.6 mg per day).

Necessary for:

Cell growth and metabolism, with the release of energy from carbohydrates, proteins, and fats in food.

Regulation of certain hormones and formation of RBCs.

Deficiencies of vitamin B_2 in the United States may be due to:

Alcohol use disorder

Poor diet

Signs of deficiency include:

Glossitis (inflammation of the tongue)

Cheilosis (cracking at corners of the mouth)

Dermatitis, photophobia, vision loss, burning or itching eyes

Vitamin B_6 (Pyridoxine)

Vitamin B_6 is a coenzyme utilized in the metabolism of carbohydrates, fats, proteins, and amino acids. It is found in meats, fish, poultry, legumes, peanuts, soybeans, wheat germ, whole-grain cereals, and bananas (DRI: 1.3–1.9 mg per day). There is significant loss of vitamin B_6 when foods are frozen.

Deficiencies may be due to:

Alcohol use disorder

Cirrhosis

Malabsorption syndromes

Signs of deficiency include:

Seizure activity in infants

Neuritis, dermatitis, nausea, vomiting, and depression in adults

Peripheral neuropathy

Caution

Overdose in those who are pregnant may result in newborns with seizures who have developed a need for greater-than-normal amounts of pyridoxine.

Patient Education

Patients taking levodopa alone (not combined with carbidopa) should be instructed not to take vitamin B_6 supplement because it antagonizes the action of levodopa.

Vitamin B_{12} (Cobalamin, Cyanocobalamin)

Vitamin B_{12} is found in meats (especially organ meats), poultry, fish and shellfish, milk, cheese, and eggs (DRI: 2.4 mcg per day). Absorption of vitamin B_{12} depends on intrinsic factor, which is normally present in the gastric juice of humans. Absence of this factor leads to vitamin B_{12} deficiency and pernicious anemia.

The National Academy of Sciences suggests that all Americans over the age of 50 begin taking a low-dose vitamin B_{12} supplement or regularly eat breakfast cereals that are fortified with the vitamin. The problem in older adults results from a reduced ability to absorb vitamin B_{12}. This is especially true for those taking medications that reduce gastric acid, for example, cimetidine (Tagamet) or omeprazole (Prilosec).

Necessary for maturation of RBCs and maintenance of the nervous system.

Deficiencies can be associated with:

Vegetarian diets without meat, eggs, or milk products
Gastrectomy or intestinal resections
Malabsorption syndromes
Pernicious anemia

Signs of deficiency include:

Anemia and weakness (first symptoms of clinical deficiency)
Poor muscle coordination
Numbness of hands and feet (paresthesia)
Mental confusion, disorientation, memory loss, and irritability

Treatment for pernicious anemia consists of vitamin B_{12} and cyanocobalamin, 100–1,000 mcg intramuscularly (IM) monthly for life to prevent neurological damage.

Side effects include:

Transient diarrhea
Itching and urticaria
❗ Anaphylaxis (rare)

Interactions may occur (decreased absorption of B_{12}) with:

Neomycin

Patient Education

Patients should avoid taking large doses of vitamin B_{12} without confirmed deficiency, as megadoses may mask the symptoms of folic acid deficiency or cause complications in those with cardiac problems or gout.

Folic Acid (Folate, Vitamin B_9)

Folic acid is a vitamin included in the B-complex group and is found in leafy and green vegetables (broccoli), avocados, beets, orange juice, kidney beans, and organ meats (DRI: 400 mcg per day). Folic acid is lost through overcooking and reheating.

Necessary for protein synthesis, production of RBCs, cell division, and normal growth and maintenance of all cells. Deficiency during pregnancy can result in neural tube defects, such as spina bifida, in the newborn.

Deficiencies can be associated with:

- Improper diet
- Alcohol use disorder
- Liver pathology
- Intestinal obstruction
- Malabsorption syndromes, malnutrition
- Renal dialysis or prolonged use of some medications (refer to listed interactions)

Signs of deficiency include:

- Anorexia, weight loss, weakness, and fatigue
- Irritability and behavior disorders
- Anemia

Interactions of folic acid, over the DRI, could interfere with the action of the following drugs:

- Phenytoin (Dilantin)
- Methotrexate
- Trimethoprim
- Triamterene

Caution

Folic acid *should not be given to anyone with potential anemia* because it may mask the diagnosis of pernicious anemia. Over-the-counter (OTC) vitamin supplements should contain no more than 0.4 mg; however, 1-mg doses are available by prescription.

Patient Education

Patients should avoid taking folic acid supplements without consulting a physician first.

Niacin (Nicotinic Acid, Niacinamide, Vitamin B_3)

Niacin is a vitamin included in the B-complex group and is found in meat, chicken, milk, eggs, fish, green vegetables, cooked dried beans and peas, soybeans, nuts, peanut butter, and enriched cereal products (DRI: 14–18 mg per day).

Necessary for lipid metabolism and nerve functioning, especially in the circulation and maintenance of all cells.

Deficiency results in pellagra, a severe skin and mucous membrane disorder that progresses to systemic and central nervous system disorders.

Signs of niacin deficiency include:

- Peripheral vascular insufficiency
- Dermatitis and varicose ulcers
- Diarrhea
- Dementia, hallucinations, depression
- Mouth sores
- Lethargy, weakness, anorexia, indigestion

Niacin is used primarily to prevent and treat pellagra. Other treatment conditions (usually as an adjunct with other medications) include:

- Many vascular disorders (e.g., vascular spasm, arteriosclerosis, Raynaud's disease, angina, varicose veins, and pressure ulcers)
- Circulatory disturbances of the inner ear, Ménière's syndrome
- Lower blood lipid levels
- Daily doses of up to 1,000 mg appear to be safe.

Side effects of niacin, especially over 1,000 mg daily, can include:

- ❗ Headache, flushing, and burning sensations of face, neck, and chest
- ❗ Postural hypotension
- ❗ Jaundice
- ❗ Nausea, diarrhea, vomiting
- ❗ Increased blood glucose and uric acid

Caution for patients with liver disease, gallbladder disease, gout, or diabetes.

Vitamin C (Ascorbic Acid)

Vitamin C is a water-soluble vitamin found in fresh fruits and vegetables, especially citrus fruits, cantaloupe, tomatoes, cabbage, green peppers, and broccoli (DRI: 75–90 mg per day). It is unstable when exposed to heat or air or combined with

Patient Education

Patients should be instructed regarding possible side effects, especially flushing and a burning sensation, and should be cautioned to rise slowly from a reclining position. They should be told that the flushing usually resolves within two weeks. Taking niacin in divided doses or extended-release products can sometimes lessen this effect. Sometimes, aspirin is prescribed to counteract flushing.

alkaline compounds (e.g., antacids). Adding baking soda to vegetables for color retention destroys vitamin C. Vitamin C is considered an antioxidant (refer to the "Antioxidants" section later in this chapter).

Necessary for:

- Formation of intracellular substances (collagen)
- Normal development of teeth, gums, and bones
- Absorption of iron
- Healing of wounds and bone fractures

Deficiencies are associated with:

- Diet lacking fresh fruits and vegetables
- Alcohol use disorder
- Infections and hemodialysis
- Smoking

Signs of vitamin C deficiency (scurvy) include:

- Muscle weakness and cramping
- Sore and bleeding mouth and gums, loose teeth
- Capillary fragility (bruising); dry, scaly skin
- Poor healing

Supplements of ascorbic acid are available in capsules, tablets (extended-release), solution, chewables, or injection form. They are indicated for:

- Treatment of scurvy (adults 100–250 mg bid, children 100–300 mg per day divided doses)
- Hemodialysis patients (100–200 mg daily)
- Infants beginning at 2 to 4 weeks of age (20–50 mg per day)

Dosages larger than those recommended are to be avoided because of the potential for side effects. In addition, because ascorbic acid is water-soluble, more than 50% of the dose is excreted in the urine of normal subjects. Excretion of less than 20% of the dose over 24 h suggests vitamin C deficiency.

Side effects of large doses of vitamin C, more than the RDA, can include:

- ❗ Heartburn, abdominal cramps, nausea, vomiting, diarrhea

❗ Increased uric acid levels; may precipitate gouty arthritis

❗ Increased urinary calcium; may precipitate kidney stone formation

❗ Scurvy in neonates following large amounts taken during pregnancy

Interactions may occur with:

Aspirin, causing elevated blood levels of aspirin

Iron (excess iron absorption with excess supplementation)

Patient Education

Patients should be given the following information concerning vitamin C:

- Vitamin C is destroyed by heat and air; therefore, raw fresh fruits and vegetables are the best sources of vitamin C.
- Large quantities of supplemental vitamin C are to be avoided, unless prescribed by a physician, because of potential side effects, such as gastric irritation, increased uric acid, and kidney stone formation.
- Antacids should not be taken at the same time as vitamin C supplements because the alkaline compound neutralizes the ascorbic acid.
- Megadoses of vitamin C taken during pregnancy may cause the newborn to require larger-than-average amounts of ascorbic acid.

Table 11-1 provides a summary of fat-soluble and water-soluble vitamins.

Table 11-1 Summary of Fat-Soluble and Water-Soluble Vitamins

Name	Food Sources	Functions	Deficiency/Toxicity
Vitamin A (retinol, beta carotene)	**Animal** Oily saltwater fish Dairy products Eggs **Plants** Dark-green leafy vegetables Deep-yellow or orange fruit and vegetables	Dim light vision Maintenance of mucous membranes Growth and development of bones Healing of wounds Resistance to infection Antioxidant (beta carotene)	**Deficiency** Slowed growth Faulty bone and tooth development Night blindness Dry skin Xerophthalmia (dry eyes) Xerosis (dry mouth) **Toxicity (hypervitaminosis A)** Irritability, lethargy, headache Joint pain, myalgia Stunted growth, fetal malformations Jaundice, nausea, diarrhea Dry skin and hair

Name	Food Sources	Functions	Deficiency/Toxicity
Vitamin D (cholecalciferol)	**Animal** Fish oils Fortified milk **Plants** Fortified cereals Sunlight	Development of healthy bones and teeth Muscle function Absorption of calcium	**Deficiency** Softening bones: Rickets (in children) Osteomalacia (in adults) Poorly developed teeth Muscle spasms **Toxicity (Hypercalcemia)** Convulsions Kidney stone formation, kidney damage Muscle/bone pain Nausea, anorexia Fetal disorders
Vitamin E (tocopherol)	**Plants** Vegetable oils Seeds, nuts Wheat germ, cereals	Antioxidant Decreases platelet clumping Normal metabolism and tissue protection	**Deficiency** Destruction of RBCs, muscle weakness **Toxicity** Prolonged bleeding time Cerebral hemorrhage Increased risk of prostate cancer
Vitamin K (phytonadione)	**Animal** Egg yolk, cheese Liver **Plants** Vegetable oil Green leafy vegetables Cabbage, broccoli	Blood clotting Bone maintenance	**Deficiency** Prolonged blood clotting time Blood in urine and stool **Toxicity** Jaundice in infants
Vitamin B_1 (thiamine)	**Animal** Pork, beef, liver Oysters **Plants** Yeast Whole and enriched grains, wheat germ Beans, peas, collard greens, nuts, asparagus Oranges	Normal function of nervous and cardiovascular systems	**Deficiency** GI upset, constipation Neuritis, mental disturbance Cardiovascular problems Muscle weakness, fatigue **Toxicity** None known
Vitamin B_2 (riboflavin)	**Animal** Milk Meat, liver **Plants** Green vegetables Cereals Enriched bread Yeast	Aids in energy metabolism of glucose, fats, and amino acids	**Deficiency** Cheilosis Glossitis Photophobia, vision problems, itching eyes Dermatitis, rough skin **Toxicity** None

(*Continued*)

Table 11-1 Summary of Fat-Soluble and Water-Soluble Vitamins (*Continued*)

Name	Food Sources	Functions	Deficiency/Toxicity
Vitamin B_6 (pyridoxine)	**Animal** Pork, beef, chicken, tuna, salmon **Plants** Whole-grain cereals, wheat germ Legumes, peanuts, soybeans Bananas	Synthesis of amino acids Antibody production Maintenance of blood glucose level	**Deficiency** Anorexia, nausea, vomiting Dermatitis Neuritis, depression **Toxicity** Seizures in newborns
Vitamin B_{12} (cyanocobalamin)	**Animal** Seafood/shellfish Meat, poultry, liver Eggs Milk, cheese **Plants** None	Synthesis of RBCs Maintenance of nervous system	**Deficiency** Nerve, muscle, mental health disorders Pernicious anemia **Toxicity** None
Niacin (nicotinic acid, vitamin B_3)	**Animal** Milk Eggs Fish Poultry **Plants** Legumes, nuts Green vegetables	Lipid metabolism Nerve functioning	**Deficiency** Pellagra **Toxicity** Headache, flushing Increased blood glucose and uric acid
Folate (folic acid, vitamin B_9)	**Animal** Organ meats **Plants** Green leafy vegetables Avocados, beets Broccoli, kidney beans Orange juice	Synthesis of RBCs, leukocytes, DNA, and RNA Needed for normal growth and reproduction	**Deficiency** Increased risk of neural tube defects Macrocytic and megaloblastic anemias Irritability, behavior disorders **Toxicity** None
Vitamin C (ascorbic acid)	**Fruits** All citrus, cantaloupe **Plants** Broccoli Tomatoes Brussels sprouts Cabbage Green peppers	Development of normal teeth, gums, and bone Prevention of scurvy Formation of collagen Healing of wounds Absorption of iron Antioxidant	**Deficiency** Scurvy Poor healing Muscle cramps/weakness Ulcerated gums/mouth, loose teeth Capillary fragility (bruising) **Toxicity** Raise uric acid level, gout GI distress Kidney stone formation Rebound scurvy in neonates

Minerals

Minerals are chemical elements occurring in nature and in body fluids. The correct balance of each is required for the maintenance of health. Minerals dissolved in body fluids are called **electrolytes** because they carry positive or negative electrical charges required for body activities, such as conduction of nerve impulses, beating of the heart, skeletal muscle contraction, and absorption of nutrients from the GI tract, protein synthesis, energy production, blood formation, and many other body processes. The most common electrolytes are sodium (Na), potassium (K), and chloride (Cl). These electrolytes can be measured via a blood sample. The normal ranges for these electrolytes can be found in Table 11-2. When the electrolytes become imbalanced in the body due to dietary issues or disease processes, the patient develops symptoms that are directly related to the function of the electrolyte in the body. Table 11-2 lists common symptoms related to electrolyte imbalances.

Table 11-2 Ranges for Select Electrolytes in the Body

Normal Range	Electrolyte Abnormalities
Sodium (Na) 135–145 mEq/L	Hyponatremia (Na <135 mEq/L) • Nausea/vomiting • Headache • Confusion • Seizures Hypernatremia (Na >145 mEq/L) • Anorexia • Lethargy • Irritability • Coma
Potassium (K) 3.5–5.5 mmol/L	Hypokalemia (K <3.5 mmol/L) • Weakness, cramping • Tingling/numbness • Constipation • Palpitations Hyperkalemia (K >5.5 mmol/L) • Abnormal heart rhythms • Muscle fatigue • Paralysis • Nausea
Chloride (Cl) 96–106 mEq/L	Hypochloremia (Cl <96 mEq/L) • Often none until very low • Headache • Nausea Hyperchloremia (Cl >110 mEq/L) • Often no symptoms • Anorexia • Irritability • Coma

Necessary for:

Numerous body functions and maintaining homeostasis (body balance)

The correct ratio of fluids to electrolytes must be maintained for normal functioning of the body. Fluids and minerals are excreted every day and must be replaced with fluid and food intake.

The principal minerals in the body and their chemical symbols are sodium (Na), chloride (Cl), potassium (K), calcium (Ca), and iron (Fe).

Sodium and Chloride (NaCl)

Sodium and chloride are the principal minerals in the extracellular body fluids. The best source of sodium and chloride is table salt (NaCl).

Deficiencies of sodium and chloride are associated with:

Excessive fluid loss: bleeding, diarrhea, vomiting, or excessive perspiration

Insufficient oral intake (starvation or extended fasting)

Alkalosis (chloride deficiency)

Treatment consists of oral or IV therapy with sodium chloride (NaCl) according to needs:

Normal Saline Solution (0.9% sodium chloride)

Potassium (K)

Potassium (DRI: 4.7 g per day) is another of the principal minerals within cells. Natural sources of potassium include citrus fruits, bananas, tomatoes, potato skins, cantaloupe, avocadoes, dried fruits, cooked dried beans, and peas.

Necessary for:

Acid–base and fluid balance

Normal muscular irritability (heartbeat regulation)

Deficiencies are associated with:

Insufficient oral intake due to surgery, anorexia, or weight-reduction diets

Diarrhea or vomiting

Diabetic ketoacidosis

Diaphoresis (excessive perspiration)

Use of diuretics, especially thiazides and loop diuretics

Digoxin toxicity

Long-term use of corticosteroids or long-term use of laxatives

Kidney disease

Signs of deficiency include:

Muscular weakness, paralysis

Cardiac arrhythmias

Lethargy and fatigue, mental apathy, and confusion

Treatment consists of:

KCl given IV postoperatively or for severe dehydration (diluted according to directions)

One of the numerous oral products available, usually in effervescent tablet or powder form, to be dissolved in water or juice and taken after meals, or capsules to be swallowed (e.g., Micro-K), extended-release tablets (e.g., Klor-Con), or oral liquid preparations.

Side effects of potassium overdose can include:

Nausea, vomiting, or diarrhea

! GI bleeding, or abdominal pain

! Cardiac arrest

Pain at the injection site or phlebitis may occur during the IV administration of solutions containing 30 mEq or more potassium per liter when infused via a peripheral vein. IV solutions containing potassium should always be run at a slow rate (max of 10 mEq/h) to prevent pain or hyperkalemia.

Hyperkalemia (excessive potassium in the blood) is not likely to result from oral administration, except in the case of severe renal impairment. Care must be taken when adding potassium to IV solutions that the dilute solution is thoroughly mixed, inverted, and agitated before the solution is hung for administration. Never add potassium to hanging IV solutions. Some medications can affect potassium levels. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers can increase the amount of potassium in the body and possibly cause hyperkalemia.

Symptoms of potassium overdose can include:

! Fall in blood pressure and/or *cardiac arrhythmias* from hyperkalemia

Confusion

Caution with the use of potassium in the following conditions:

Cardiac disease

Renal impairment

Gastric or intestinal ulcers (extended-release products contraindicated)

Mental confusion (unable to follow directions properly)

Patient Education

Patients taking potassium supplements should be instructed regarding:

Natural sources of potassium-rich foods

Conditions requiring potassium supplements

Directions for taking potassium supplements with or after meals to avoid GI distress and the importance of following package directions carefully

The importance of following specific directions carefully with certain formulations that need to be dissolved in water

Notifying a physician immediately of any side effects

Calcium (Ca)

Calcium is a mineral component of bones and teeth. It is absorbed in the small intestine with the help of vitamin D. Natural sources include milk and dairy products (RDA: 1,000–1,200 mg per day). In postmenopausal women not receiving estrogen therapy, the RDA is about 1,500 mg per day. Those who are lactose intolerant (unable to take milk) should include in their diet dark-green leafy vegetables (except spinach), broccoli, and canned fish with the bones (DRI: 1,000–1,300 mg per day, with the higher figure recommended for adolescents of both sexes and postmenopausal females). The normal blood calcium level is 8.8–10.4 mg/dL.

Necessary for:

- Strong bones and teeth
- Contraction of cardiac, smooth, and skeletal muscles
- Nerve conduction
- Blood coagulation, capillary permeability, and normal blood pressure
- The balance between *dietary* calcium and magnesium is important in the prevention of heart disease.

Deficiencies (supplements required) are associated with:

- Pregnancy and lactation
- Postmenopausal females (or those with estrogen deficiency)
- Hypoparathyroidism
- Long-term use of corticosteroids, some diuretics, or anticonvulsants
- Chronic diarrhea, pancreatitis, renal failure
- Lack of weight-bearing exercise

Signs of deficiency may include:

- Osteoporosis or osteomalacia (softening of bones), including frequent fractures, especially in older adults
- Rickets in children (softening of bones)
- Muscle pathology, including cardiac myopathy or tetany (muscle spasm) and leg cramps
- Increased clotting time

Treatment consists of taking calcium supplements 400–600 mg daily PO. A higher-dosage supplement is required for those not including calcium-rich foods in the diet (e.g., without dairy products). The RDAs, *including foods,* are 1,200 mg per day for adults and 1,500 mg per day for postmenopausal females not taking estrogen. Many products and combinations are available, including calcium gluconate, calcium carbonate, and calcium lactate. Of these three, calcium carbonate delivers the highest amount of elemental calcium per tablet.

Adding vitamin D for calcium metabolism may be necessary for people without exposure to sunlight (refer to “Vitamin D”).

Side effects of calcium salts can include:

- ❗ Constipation from oral products
- Tissue irritation from IV products

When injected IV, calcium salts should be administered *very slowly* to prevent tissue necrosis or *cardiac arrhythmias.*

Emerging evidence has raised concerns (and confusion) about potential adverse effects of high calcium intake on cardiovascular health. Several recent large studies have shown that females who use *calcium supplements* had a statistically significant increase in myocardial infarctions (MIs); men experienced a significantly elevated risk of heart disease mortality. These risks have not been reported with dietary calcium, suggesting that the rapid rise in calcium concentrations with supplements may be a factor.

Caution: Calcium should be used cautiously, if at all, with:

Cardiac disease

Renal disease

Respiratory conditions (e.g., sarcoidosis)

Administration: While the most common oral calcium supplement, calcium carbonate, is best taken with meals, other calcium supplements should be administered 1–1.5 h after meals. Remember to always check the label.

Interactions may occur with:

Digoxin, resulting in potentiation (may cause arrhythmias)

Clinical Application

Patient Counseling

Vitamin D and calcium carbonate are regularly used to treat or prevent osteoporosis. Patients usually take two to three doses per day. It is important to counsel patients that the bones absorb calcium best when they are resting. This means that the most important dose is at bedtime when the patient will be lying down (sleeping) for the next 6–8 h. This is important because patients often forget doses, but reminding them that the nighttime dose is the most important can be helpful.

Patient Education

Patients taking calcium should be instructed regarding:

Calcium-rich diet, especially dairy products and vitamin D-enriched milk, which can be low-fat

Necessity for calcium supplements (including discussion of risk versus benefits), usually recommended for females beginning at age 35, and especially for postmenopausal females not on estrogen therapy

Importance of upright exercise, for example, walking at least three to four times per week to preserve bone mass

Importance of outdoor activity because sunlight helps create the vitamin D necessary for calcium metabolism

Taking calcium supplements as specified on the label

Not taking calcium at the same time as other medications

Iron (Fe)

Iron is vital for the oxygen-carrying and the oxygen-delivery component of blood. Iron is a mineral found in meat (especially liver), egg yolks, beans, spinach, enriched cereals, dried fruits, prune juice, and poultry. The DRI for iron is 8–18 mg per day.

Necessary for hemoglobin formation; 70% of the body's iron is bound to hemoglobin.

Deficiencies (supplements recommended) are associated with:

- Hemorrhage and excessive menstrual flow
- Internal bleeding, ulcers, and GI tumors
- Pregnancy
- Infancy
- Puberty at the time of growth spurt
- Patients undergoing hemodialysis

Signs of deficiency may include:

- Paleness of the skin and/or mucous membranes
- Lethargy and weakness
- Vertigo (dizziness, lightheadedness)
- Air hunger
- Decline in mental skills
- Irregular heartbeat and function
- Cravings for nonfood items, for example, ice, clay, or starch (called pica)

Treatment of anemia due to iron deficiency consists of administration of iron preparations

Side effects of taking iron preparations can include:

- ❗ Black stools
- ❗ Nausea and vomiting (GI effects can be minimized by taking iron after or with meals, *but not with coffee, tea, or milk*)
- ❗ Constipation or diarrhea
- Anaphylactic reactions or phlebitis with IV administration of iron dextran

Contraindicated in patients with peptic ulcer, regional enteritis, or ulcerative colitis.

- Parenteral iron should *not* be administered concomitantly with oral iron therapy.
- Iron should *not* be administered without confirming a diagnosis of deficiency with a blood test and determining the cause of deficiency.

Interactions may occur with:

- Vitamin C or orange juice, taken at the same time, which *enhances* iron absorption

Symptoms of acute overdose of iron may occur within minutes or days and include:

- Lethargy
- ❗ Shock

Patient Education

Patients taking iron supplements should be instructed regarding:

- *Avoidance of self-medication* without established need (blood test) and without medical supervision to determine why hemoglobin level is low; taking iron when not prescribed could mask the symptoms of internal bleeding or GI malignancy
- Black stools to be expected
- Taking iron at meals to minimize GI distress and with orange juice for better absorption
- *Interactions* (i.e., avoidance of coffee, tea, milk, or antacids at the same time)

Caution with flavored children's tablets (overdosage can be dangerous, even fatal)

Taking liquid iron preparations with a drinking straw to avoid temporary stain of dental enamel

The iron in meats is called heme iron and is better absorbed than nonheme iron in vegetables and fruits

Nonheme iron is absorbed better if consumed with meat proteins or a rich source of vitamin C (e.g., orange juice)

Zinc (Zn)

Zinc is a component of numerous enzymes and is an essential element in metabolism. It is usually found in adequate amounts in a well-balanced diet. Rich sources include lean meat, organ meats, oysters, poultry, fish, and whole-grain breads and cereals (DRI: 8–11 mg per day). Zinc is an antioxidant.

Necessary for:

- Wound healing
- Mineralization of bone
- Insulin production and glucose regulation
- Normal taste

Deficiencies (supplements recommended) are associated with:

- Inadequate or vegetarian diet
- Chronic, nonhealing wounds
- Major surgery or trauma

Deficiency symptoms can include:

- Poor wound healing
- Reduced taste perception
- Poor alcohol tolerance, glucose intolerance
- Anemia, slowed growth, sterility
- Dermatitis and hair loss

Toxicity (more than 2 g per day) may cause:

- Nausea, GI distress, vomiting

Treatment consists of tablets or capsules administered with meals tid to minimize gastric distress. Standard supplement of zinc is no more than 11 mg/24 h. If a zinc supplement is required for more than 90 days, blood levels should be monitored. Chronic consumption of high levels of zinc may cause copper deficiency.

Many combinations of various vitamins and minerals are available in OTC products with various strengths and forms.

Respiratory Illness Recovery and Prevention

Vitamins and Minerals

During the COVID-19 global pandemic, researchers and physicians recommended vitamins B, C, D, and zinc to help fight the virus. Zinc is known to help shorten the length of the common cold and helps alleviate nasal congestion, drainage, sore throat, and cough. Zinc has also been shown in research to activate T cells, which are part of the immune response. Many products are available over the counter to help boost the immune system to help prevent or shorten illness burden.

Table 11-3 provides a summary of the major minerals.

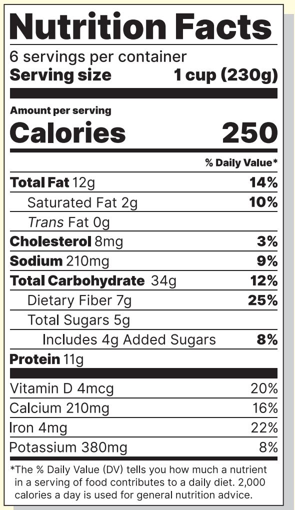
Table 11-3 Summary of Major Minerals

Name	Food Sources	Functions	Deficiency/Toxicity
Calcium (Ca) (DRI: 1,000–1,300 mg per day)	Milk, cheese, yogurt Sardines Salmon Green vegetables except spinach	Development of bones and teeth Contraction of cardiac, smooth, and skeletal muscles Nerve conduction Blood clotting	**Deficiency** Osteoporosis, osteomalacia Rickets (in children) Muscle pathology Heart disease Increased clotting time **Toxicity** Kidney stones
Potassium (K) (DRI: 4.7 g per day)	Oranges, bananas Dried fruits Tomatoes	Contraction of muscles Heartbeat regulation Transmission of nerve impulses Maintaining fluid balance	**Deficiency (hypokalemia)** Muscle weakness Cardiac arrhythmias Lethargy, mental confusion **Toxicity (hyperkalemia)** Weakness Cardiac arrhythmias
Sodium (Na) (DRI: 1,300– 1,500 mg per day)	Table salt Beef, eggs Milk, cheese	Maintaining fluid balance in blood Transmission of nerve impulses	**Deficiency** Low blood pressure **Toxicity** High blood pressure
Chloride (Cl) (DRI: 1.8–2.3 g per day)	Table salt	Gastric acidity Regulation of osmotic pressure Activation of salivary amylase	**Deficiency** Imbalance in gastric acidity Imbalance in blood pH **Toxicity** Diarrhea
Magnesium (Mg) (DRI: 320– 420 mg)	Green vegetables Whole grains	Synthesis of ATP (adenosine triphosphate) Transmission of nerve impulses Relaxation of skeletal muscles	**Deficiency (seldom)** Imbalance Weakness **Toxicity** Diarrhea

Name	Food Sources	Functions	Deficiency/Toxicity
Iron (Fe) (DRI: 8–18 mg per day)	Meat Liver Eggs Poultry Spinach Dried fruits Dried beans Prune juice	Hemoglobin formation	**Deficiency (anemia)** Paleness Lethargy Air hunger Irregular heartbeat **Toxicity** Lethargy, shock Vomiting, diarrhea Erosion of GI tract Liver or kidney damage
Iodine (I) (DRI: 150 mcg per day)	Freshwater shellfish and seafood Iodized salt	Major component of thyroid hormones Regulates rate of metabolism Growth, reproduction Nerve and muscle function Skin and hair growth	**Deficiency** Goiter Hypothyroidism **Toxicity** "Iodine goiter" Hyperactive, enlarged goiter
Zinc (Zn) (DRI: 8–11 mg per day)	Meat Liver Oysters Poultry Fish Whole-grain bread and cereal	Wound healing Mineralization of bone Insulin and glucose regulation Normal taste Antioxidant	**Deficiency** Poor wound healing Reduced taste perception Alcohol/glucose intolerance **Toxicity** GI distress Copper deficiency with extended use of high levels of zinc

Patient Education

Food labels provide a nutritional analysis of the food product. The Percentage (%) Daily Value is the amount of the nutrient obtained by eating the equivalent of one serving of the product. The amount is given in a percentage based upon a 2,000-calorie daily diet. Be careful as the serving per container can make a big difference. As shown in Figure 11-1, this container has 6 servings.



Nutrition Facts

6 servings per container
Serving size **1 cup (230g)**

Amount per serving
Calories **250**

	% Daily Value*
Total Fat 12g	**14%**
Saturated Fat 2g	**10%**
Trans Fat 0g	
Cholesterol 8mg	**3%**
Sodium 210mg	**9%**
Total Carbohydrate 34g	**12%**
Dietary Fiber 7g	**25%**
Total Sugars 5g	
Includes 4g Added Sugars	**8%**
Protein 11g	
Vitamin D 4mcg	20%
Calcium 210mg	16%
Iron 4mg	22%
Potassium 380mg	8%

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

maradaisy/Shutterstock.com.

Figure 11-1 Nutrition facts.

Antioxidants

No discussion of nutrition would be complete without an explanation of antioxidants, as we know them. **Antioxidants**, sometimes referred to as "anticancer foods" or "natural drugs," inhibit cell destruction in damaged or aging tissues caused by unstable molecules known as free radicals. Although free radical damage may lead to cancer, and laboratory evidence suggests that antioxidants may slow or possibly prevent cancer, several large-scale clinical trials on the use of antioxidants have not shown a decrease in the risk of cancer (or heart disease and other conditions).

Free radicals attack the cells, causing damage that prevents the transport of nutrients, oxygen, and water into the cells and the removal of waste products. This damage affects the nucleic acids in their function of growth and repair of tissues. Free radical damage is associated with several age-related diseases. For example, damage to the nucleic acids might initiate the growth of abnormal cells, the first step in cancer development. Also, free radical attack to the cell membranes of the tissues lining the blood vessels can lead to cholesterol accumulation in the damaged arteries, the initial state of atherosclerosis and heart disease. In addition, free radicals are associated with inflammation, drug-induced organ damage, immunosuppression, and possibly other disorders as well.

The body has developed an antioxidant system response to defend itself from free radicals. An antioxidant is defined as any compound that fights against the destructive effects of free radical oxidants. This system is comprised of enzymes, vitamins, and minerals. Antioxidants function in the prevention of free radical formation by binding to, and neutralizing, destructive substances before they damage cells and tissues.

The antioxidant vitamins—*vitamin C, vitamin E,* and *beta carotene*—can function independently of enzymes. Antioxidant minerals include copper, manganese, selenium, and zinc. These minerals work with antioxidant enzymes and are essential for proper enzyme function. If the diet is inadequate in these minerals, the enzymes are not produced or are ineffective.

Caution

Taking antioxidants while undergoing chemotherapy or radiation treatments could be contraindicated. Chemotherapy and radiation generate free radicals, and they need an oxidative process to actually kill tumor cells. By giving antioxidants concurrently with chemotherapy or radiation, you actually can increase the tumor cell's life. It is recommended that patients stop taking antioxidants two days before chemotherapy or radiation and avoid them during the treatment and for two days after completion of the treatment.

Patient Education

Patients asking about antioxidants should be instructed regarding:

- Foods that provide antioxidant action
- Natural antioxidants in certain foods, which are more effective than synthetic products
- When antioxidants are contraindicated and the health problems with megadosing

Alternative Medicines

Herbs and Other Dietary Supplements

As a health care professional, you may be asked about dietary supplements and about **herbal** remedies. It is important for you to be able to answer these questions effectively and refer your patients to reliable sources of information. There are many books on the market and articles on the Internet describing the use of herbal remedies. In assessing the value of these resources, question the source, the credentials of the author, the research involved in collecting the data, and the reliability and validity of the statistics. Be sure that the information is based on fact, not opinion. You have a responsibility to caution your patients regarding the dangers of taking remedies not approved by the FDA and especially the risk of possible interactions between "natural products" and prescription drugs.

In April 2005 (updated April 7, 2012) the FDA published a report entitled *Guidance for Industry: A Dietary Supplement Labeling Guide,* which answers many questions on the labeling of dietary supplements. In February 2009 (updated March 2013), the National Center of Complementary and Alternative Medicine at the National Institutes of Health published a fact sheet entitled *Get the Facts: Using Dietary Supplements Wisely*. The following information is taken from these materials.

Congress passed the Dietary Supplement Health and Education Act (DSHEA) of 1994, which amended the Food, Drug, and Cosmetic Act to recognize dietary supplements as distinct from food additives and drugs, which are monitored and regulated by the FDA. *Food supplements are not subject to the same scrutiny and restrictions*, so consumers and manufacturers are responsible for checking the safety of dietary supplements and determining the truthfulness of label claims.

CBD

Cannabidiol (CBD) is a chemical in the *Cannabis sativa* plant, also known as marijuana or hemp. While delta-9-tetrahydrocannabinol (THC) is the major active ingredient in marijuana, cannabidiol (CBD) is also obtained from hemp, which contains very small amounts of THC. Hemp-derived products contain no more than 0.3% THC on a dry-weight basis. All 50 states have laws legalizing CBD with varying restrictions. CBD and hemp oils do not contain enough of the psychoactive compound THC to produce a "high." CBD is nonpsychoactive, which means it does not alter mental state, but it does have a number of the same medical benefits as THC.

Evidence is limited for some forms of CBD, but there is some data to support the beneficial effects and adverse effects listed in the following text. In fact, Epidiolex, primarily consisting of CBD, is the first FDA-approved medication for seizures. Advise patients to obtain CBD from a reputable source and to discuss its use with their physician.

Potential Beneficial Effects of CBD

- Analgesia
- Anticonvulsant
- Antioxidant
- Anxiolytic and antipsychotic
- Muscle relaxant
- Neuroprotective

Potential Adverse Effects of CBD

- Decreased appetite
- Weight loss
- Diarrhea
- Dizziness, drowsiness
- Fatigue
- Liver injury (more likely with 20 mg/kg/day dose or in combination with clobazam or valproate)

Common Forms of CBD

Oils and tinctures	• Placed under the tongue with a dropper • Absorbed quickly • Good for patients who cannot swallow tablets or capsules
Creams and lotions	• Used to treat muscle and joint pain • Can also be used for some skin conditions like eczema and psoriasis
Capsules and tablets	• Used for systemic treatment of seizure disorder and digestive issues • Also used for nausea and analgesia
Edibles	• Most common form is gummies • Appropriate for patients who cannot swallow tablets or capsules
Vaping	• Inhaling CBD is the fastest way to experience effects; however, the effects of, and damage caused to the respiratory system by, vaping must be considered • Used for anxiety, analgesia, and so on

Dietary Supplements

Patients may be ordered nutritional supplements. These include flavored drinks such as Ensure and ProStat. These drinks contain high amounts of protein to help with healing. These supplements are ideal for those with poor appetites due to their disease or treatment.

The term *dietary supplements* has traditionally referred to products made of one or more of the essential nutrients, such as vitamins, minerals, and proteins. DSHEA broadens the definition to include, with some exceptions, any product intended for ingestion as a supplement to the diet. This includes vitamins; minerals; herbs; botanicals; other plant-derived substances; amino acids (the individual building blocks of protein); and concentrates, metabolites, constituents, and extracts of these substances.

It is easy to spot a supplement because DSHEA requires manufacturers to include the words *dietary supplement* on product labels. Also, since March 1999, a “Supplement Facts” panel is required on the labels of most dietary supplements. The supplement manufacturers are required to document substantiation of their claims. They must also include a disclaimer on their labels that the dietary supplements *are not drugs and received no FDA premarket approval*. The rule, published in the January 6, 2000 *Federal Register*, also prohibits “structure/function” claims (claims that the products affect the structure or function of the body) without prior FDA review. Supplement labels also *may not, without prior FDA review, bear a claim that they can prevent, treat, cure, mitigate, or diagnose a disease*.

Drugs used as traditional medicines are sometimes derived from plants. However, before marketing and FDA approval, they must undergo extensive clinical studies to determine their effectiveness, safety, possible interactions, and appropriate dosages. *The FDA does not authorize or test dietary supplements.*

Dietary supplements are available in many forms, including tablets, capsules, powders, softgels, gelcaps, and liquids. Though commonly associated with health food stores, dietary supplements also are sold in grocery, drug, and national discount chain stores, as well as through mail-order catalogs, TV programs, the Internet, and direct sales.

Under DSHEA, once a dietary supplement is marketed, the FDA is responsible for showing that a dietary supplement is *unsafe* before it can take action to restrict the product's use. This was the case when in June 1997, the FDA proposed, among other things, to limit the amount of ephedrine alkaloids in dietary supplements (marketed as, e.g., ephedra, ma huang, and epitonin) and provide warnings to consumers about the hazards associated with the use of dietary supplements containing these ingredients. The hazards ranged from nervousness, dizziness, and changes in blood pressure and heart rate to chest pain, heart attack, hepatitis, stroke, seizures, psychosis, and death. The proposal stemmed from the FDA's review of adverse event reports it had received, scientific literature, and public comments. Finally, in 2004, the FDA announced a ban on the weight-loss aid ephedra. However, there are numerous other dangerous supplements still on the market.

In September 2010, *Consumer Reports* identified a dozen supplements that—according to government warnings and adverse-event reports—were too dangerous to be on the market. However several years after this report, the following unsafe supplements were still available in retail stores or by shopping online: *germanium* (linked to kidney failure and death); *yohimbe* (linked to heart and blood pressure problems); *bitter orange* (linked to arrhythmias, heart attacks, and stroke); and *chapparal, comfrey,* and *kava* (linked to liver failure).

Fraudulent Products

Consumers need to be aware of fraudulent products. These are products that do not do what they say they can or do not contain what they say they contain. At the very least, they waste consumers' money, and they may cause physical harm. Fraudulent products often can be identified by the types of claims made in their labeling, advertising, and promotional literature. Some possible indicators of fraud, says Stephen Barrett, MD, a board member of the National Council Against Health Fraud, are as follows:

- Claims that the product is a secret cure and use of such terms as *breakthrough*, magical, miracle cure, and *new discovery*. "If the product were a cure for a serious disease, it would be widely reported in the media and used by health care professionals," he says.
- Claims that a product is backed by scientific studies, but with no list of references or references that are inadequate. For instance, if a list of references is provided, the citations cannot be traced, or if the references are traceable, the studies are out of date, irrelevant, or poorly designed.

Quality Products

The growing market for supplements, with fewer regulations, creates the potential for quality-control problems. For example, the FDA has identified several manufacturers that were buying herbs, plants, and other ingredients without first adequately testing them to determine whether the product they ordered was actually what they received or whether the ingredients were free from contaminants and were of the strength stated.

To help protect themselves, consumers should:

- Ensure that ingredients in products have the U.S. Pharmacopeia (USP) notation, which indicates that the manufacturer followed the standards established by the USP.
- Realize that the label term *natural* does not guarantee that a product is safe. “Think of poisonous mushrooms,” says Elizabeth Yetley, PhD, director of the FDA’s Office of Special Nutritionals. “They’re natural.”
- Consider the name of the manufacturer or distributor. Supplements made by a nationally known food and drug manufacturer, for example, have been made under tight controls because these companies already have manufacturing standards in place for their other products.
- Write to the supplement manufacturer for more information. Ask the company about the conditions under which its products were made.
- Avoid products sold for considerably less money than competing brands.

Reading and Reporting

Consumers who use dietary supplements should always read product labels, follow directions, and heed all warnings.

Supplement users who experience a serious harmful effect or illness that they think is related to the use of supplements should call a physician or other health care professional. They, in turn, can report it to the FDA MedWatch by calling 1-800-FDA-1088 or on the MedWatch website at https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program. Patients’ names are kept confidential.

Much regarding the health benefits and potential risks of many dietary supplements remains unknown. Therefore, consumers who decide to take advantage of the expanding market should do so with care, making sure to have the necessary information and consulting with their physicians regarding any health conditions that could be compromised or any medications they are taking that may interact adversely with the supplements. “The majority of supplement manufacturers are responsible and careful,” the FDA’s Yetley says. “But, as with all products on the market, consumers need to be discriminating. FDA and industry have important roles to play, but consumers must take responsibility, too.”

Your responsibility as a health care professional includes warning your patients, and others who may seek your advice, regarding the dangers of taking products not approved by the FDA and not adequately tested. You must also caution them about the possibility of fraudulent products and lack of quality control. Most important, you must warn them about possible interactions with the medicines they are taking and the potential for serious adverse reactions. All the herbal remedies on the market are too numerous to mention in this chapter. However, you will find some of the more popular ones, along with cautions or interactions known at this time, listed in Table 11-4. Table 11-4 provides a list of some herbs, possible uses, cautions, and interactions.

Table 11-4 Herbs

Herbs	Possible Uses	Possible Side Effects, Cautions, and Interactions
Ashwagandha	Used to improve thinking ability, decrease pain and swelling (inflammation), and prevent the effects of aging; also used for fertility problems in males and females and to increase sexual desire	Short-term use only; large doses may cause stomach upset, vomiting, and diarrhea; interacts with thyroid medication; may increase the symptoms of autoimmune diseases; do not use during pregnancy or lactation; stop taking at least two weeks before surgery
Astragalus	Used alone or with other herbs to support or enhance the immune system	May interact with medications that suppress the immune system; may affect blood sugar levels and blood pressure; some *Astragalus* species, normally not used in dietary supplements, may be toxic
Cascara sagrada	Relieves occasional constipation	Do not use if appendicitis, rectal bleeding, diarrhea, or a history of stomach or intestinal problems (e.g., blockage, inflammation, ulcers, Crohn's disease, bleeding, severe constipation) are present; if recent abdominal surgery has been performed; if pregnant or breastfeeding; or if heart problems are present Interacts with digoxin
Cat's claw	Anti-inflammatory used for osteoarthritis and rheumatoid arthritis; antiviral used for treatment of viral infections such as shingles and cold sores	Affect medications changed by the liver, medications that suppress the immune system, and antihypertensive medications; take with caution; may cause hypotensive episodes; may worsen leukemia; may increase the symptoms of autoimmune diseases; do not use if pregnant or breastfeeding; stop taking two weeks before surgery
Cinnamon	Lowers blood sugar; alleviates gas and muscle and stomach spasms; prevents nausea, vomiting, diarrhea; used to treat infections, such as the common cold	Short-term use only; unsafe when taken in large amounts or long term; may cause skin irritation or allergic reaction when applied to skin; do not use if pregnant or breastfeeding; may affect blood sugar levels; observe for hypoglycemia; monitor blood sugar; may damage the liver; do not use with liver disease; interacts with antidiabetic medications; stop taking two weeks before surgery
Cranberry	Antibacterial, prevents urinary tract infections (UTIs)	Do not use with active UTI
Chamomile	Sedative tea, prevents insomnia nausea	Those allergic to pollens, for example, ragweed, may be allergic to it
Echinacea	Proven ineffective in 2005 studies for prevention and treatment of colds	Can cause allergies and rashes Contraindicated in those with autoimmune diseases, for example, human immunodeficiency virus, MS, or lupus, and chronic use, longer than eight weeks

(*Continued*)

Table 11-4 Herbs (*Continued*)

Herbs	Possible Uses	Possible Side Effects, Cautions, and Interactions
Elderberry	Treatment of the flu; may reduce inflammation	Possibly safe when used for up to five days; not for long-term use; raw and unripe fruit may cause nausea, vomiting, and severe diarrhea; do not use if pregnant or breastfeeding; may increase the symptoms of autoimmune diseases; may interact with medications that suppress the immune system
Fenugreek	May lower blood sugar, cholesterol, and triglycerides May reduce symptoms of heartburn	Interacts with antidiabetic medications, warfarin, anticoagulants, and antiplatelets; likely safe for people when taken by mouth in amounts normally found in foods; side effects include diarrhea, stomach upset, bloating, gas, a “maple syrup” odor in urine; likely unsafe for children or those who are pregnant or breastfeeding; might cause early labor; may affect blood sugar levels in people with diabetes; observe for signs of hypoglycemia; monitor blood sugar carefully
Garlic	Taken to lower blood pressure and cholesterol Anti-infective, immune enhancing	Risk of bleeding with anticoagulants Nausea, vomiting, diarrhea, heartburn, and flatulence
Ginger	Prevents nausea, motion sickness	Doses higher than 6 g can cause gastric irritation
Ginkgo (GBE)	Used as antidepressant, anxiolytic, and antioxidant Proven ineffective in a 2008 study for prevention or slowing of dementia or Alzheimer’s disease	May interact with anticoagulants to cause bleeding and strokes Rare GI upset, headache
Ginseng	Antistress, antifatigue agent	Not for long-term use May cause hypertension, nausea, vomiting, diarrhea, nervousness, mental changes Contraindicated in pregnancy
Glucosamine	Anti-inflammatory for arthritis	Elevated cholesterol Insulin resistance, higher blood glucose
Goldenseal	Antibacterial, antiparasitic agent	Short-term use only May cause nausea and vomiting May alter the way body processes medications Use with caution
Kava	FDA warning March 2002 Banned in Canada, Germany, South Africa, and Switzerland	Possible liver damage, often irreversible; deaths reported
Milk thistle	Anti-inflammatory, liver protectant, aids in regeneration of liver cells	No harmful effects if taken at normal recommended doses

Herbs	Possible Uses	Possible Side Effects, Cautions, and Interactions
Peppermint	Treats indigestion and stomach upset, treats colds and congestion, and relieves pain when applied topically	Do not use in babies because it may cause choking Do not inhale for prolonged periods of time
Saw palmetto	Taken for benign prostatic hyperplasia (BPH) Antiandrogen	Rare GI upset Visit a physician for diagnosis and treatment
Turmeric	Taken for stomach upset, osteoarthritis	Usually does not cause significant side effects. May make gallbladder problems worse; may interact with anticoagulant/antiplatelet drugs; do not take if pregnant or breastfeeding; stop taking two weeks before surgery
Valerian	Taken for anxiety, insomnia	Morning-after drowsiness Avoid during pregnancy Short-term use only

Patient Education

Dietary Supplements

Patients should be instructed regarding the following:

- Consulting a physician or pharmacist before taking any "herbal remedies." Some herbs may be contraindicated with certain diagnoses.
- Taking a list of all products you are using, including herbal remedies, herbal teas, vitamins and minerals, OTC (nonprescription) medicines, and prescription drugs, to a physician or pharmacist. Many of these products can interact, with dangerous, even life-threatening, results. Consulting a physician is important before starting any "alternative medicines." Do not mix prescription drugs and herbal remedies for the same condition.
- The fact that *natural* does not mean "safe."
- Not taking more than the recommended amount listed on the label. Even vitamins and minerals in excess of the RDA or DRI can cause serious problems. Herbs that may be safe in small doses could be harmful at larger doses or over a prolonged period of time. Products without dosage recommendations should be avoided.
- All products should carry a lot number; expiration date; and manufacturer's name, address, and phone number. Products should be *avoided* that lack this information or that claim an effect on the body's structure or function or claim to be able to cure a disease or condition.
- Storing herbal products away from young children and pets.
- Not using herbal products for children without the approval of a pediatrician.
- Not using herbal remedies if you are pregnant, trying to become pregnant, or nursing.
- Not taking these products with alcohol without first determining the safety of such a combination.
- Not using these products as a substitute for proper rest and nutrition. A balanced diet is necessary for good health.

Suggested Readings

National Center for Complementary and Integrative Health. *Complimentary, alternative or integrative health: What's in a name?* Retrieved from https://nccih.nih.gov/health/integrative-health

National Center for Complementary and Alternative Medicine. *Get the facts: Using dietary supplements wisely*. Retrieved from Using Dietary Supplements Wisely https://www.nccih.nih.gov/health/using-dietary-supplements-wisely

U.S. Food and Drug Administration (April 2005). *Dietary supplements.* Retrieved from http://www.fda.gov/Food/DietarySupplements/default.htm

WebMD. *Find a vitamin or supplement: Ashwagandha*. Retrieved from https://www.webmd.com/vitamins/ai/ingredientmono-953/ashwagandhaWebMD. *Find a vitamin or supplement: Cassis cinnamon.* Retrieved https://www.webmd.com/vitamins/ai/ingredientmono-1002/cassia-cinnamonWebMD. *Find a vitamin or supplement: Cat's claw*. Retrieved from https://www.webmd.com/vitamins/ai/ingredientmono-395/cats-clawWebMD. *Find a vitamin or supplement: Elderberry*. Retrieved https://www.webmd.com/vitamins/ai/ingredientmono-434/elderberryWebMD. *Find a vitamin or supplement: Fenugreek*. Retrieved from https://www.webmd.com/vitamins/ai/ingredientmono-733/fenugreekWebMD. *Find a vitamin or supplement: Turmeric*. Retrieved from https://www.webmd.com/vitamins/ai/ingredientmono-662/turmeric

Case Study A

Water-Soluble Vitamins

A 37-year-old patient who is pregnant is at the OB-GYN's office for a 16-week checkup.

1. The physician is reviewing the patient's diet and inquires about their intake of folic acid. A deficiency in folic acid during pregnancy can result in which condition in newborns?

a. cerebral palsy
b. cardiac malformations
c. spina bifida
d. seizures

2. Which of the following foods is richest in folic acid?

a. radishes
b. black beans
c. broccoli
d. alfalfa sprouts

3. Why is folic acid a necessary supplement for those who are pregnant?

a. for the production of RBCs
b. for fat metabolism
c. for cell mitosis
d. for the destruction of white blood cells (WBCs)

4. Which of the following is a sign of a folic acid deficiency?

a. weight gain
b. muscle cramps
c. pale sclera
d. weight loss

5. The physician cautions the patient about the amount of daily folic acid supplementation. What is recommended as the maximum amount of folic acid intake per day?

a. 0.4 mg
b. 0.8 mg
c. 1.2 mg
d. 5 mg

Case Study B

Minerals

A seventy-three-year-old patient has started taking a loop diuretic to reduce their elevated blood pressure.

1. While taking this specific high blood pressure medication, the patient is at risk for developing a deficiency in which mineral?

a. potassium (K)
b. chloride (Cl)
c. calcium (Ca)
d. iron (Fe)

2. Which of the following may result from a deficiency of K?

a. anorexia
b. muscular weakness
c. hypothermia
d. constipation

3. What is one symptom of K overdose?

a. hypokalemia
b. shortness of breath
c. urinary retention
d. cardiac arrest

4. While taking a potassium supplement, the patient experiences some GI distress. When should they take the K^+ to minimize these GI side effects?

a. with or after meals
b. just before bed
c. upon rising in the morning
d. two hours prior to a meal

5. Which of the following will provide the patient with the best source of K?

a. carrot salad
b. broccoli rabe saute
c. fruit salad
d. green beans

Chapter Review Quiz

Multiple Choice

1. Antioxidants

a. are safe to take in megadoses
b. consist of proteins, carbohydrates, and fats
c. are found only in synthetic products
d. fight against the destructive effects of free radicals

2. Free radical damage can be associated with

a. stunted growth
b. glaucoma
c. heart disease
d. grand mal seizure

3. Which of the following is an antioxidant vitamin?

a. calcium
b. beta carotene
c. folate
d. niacin

4. Which of the following is an antioxidant mineral?

a. potassium
b. sodium
c. zinc
d. iron

5. Signs of a vitamin A deficiency may include which of the following?

a. watery eyes
b. night blindness
c. weight gain
d. accelerated growth

6. When buying dietary supplements, you should look for which term on the label?

a. natural
b. FDA
c. USP
d. new discovery

7. Which of the following herbs can interact with anticoagulants to cause bleeding?

a. cranberry and milk thistle
b. garlic and ginkgo
c. saw palmetto and glucosamine
d. ginseng and echinacea

8. Glucosamine

a. is always combined with chondroitin
b. has no known side effects
c. can elevate cholesterol level
d. counteracts thyroid medicine

9. Garlic

a. lowers blood pressure and cholesterol level
b. helps to control menopause symptoms
c. alleviates symptoms of depression
d. was banned by the FDA due to the danger of heart problems and stroke

10. Ginseng

a. interacts with oral contraceptives
b. has no known side effects
c. causes liver damage
d. may cause hypertension, mental changes, and nervousness

Chapter 12

Integumentary System Medications

Key Terms and Concepts

Antifungals
Antipruritics
Antiseptics
Antiviral
Bactericidal
Emollients
Immunomodulators
Keratolytic
Protectants

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe proper application procedures for various skin medications.
2. Identify indications, side effects, and precautions or contraindications of the nine major categories of skin medications.
3. Explain the factors that influence the absorption of skin medications.
4. Classify drugs according to their action: antipruritic, emollient, keratolytic, enzymatic, antifungal, anti-infective, or agents to treat burns and acne.
5. Identify appropriate indications of the nine major categories of skin medications.

The integumentary system consists of the skin, hair, nails, and exocrine glands. Although the skin is only a few millimeters thick, it is the body's largest organ. It is the external covering of the body that serves to protect the inner organs from damage such as abrasions, burns, dehydration, and UV rays. Nails also act as a barrier to damage and are located specifically in areas of the body (such as fingers and toes) that frequently come into contact with abrasive surfaces. The skin contains sweat glands that function to regulate body temperature by secreting sweat, which evaporates on the surface of the skin and helps the body cool down. The skin also signals that the body is getting cold by forming goosebumps, which has the effect of making body hair stand out from the skin to trap more air to act as insulation.

There are many conditions that can affect the skin, causing pain, irritation, and discomfort. Skin ailments can range from minor ones, such as pruritus (itching), to major ones, such as severe burns. Treatment is usually topical or local (applied to the affected area), but skin conditions are sometimes treated internally with oral medications or injections for their systemic effects. Some skin conditions are caused by inflammation or immunologic alterations in the cells of the skin. These conditions have led to the development of newer medications, some of which are classified as **immunomodulators**.

This chapter primarily explains topical medications. Medications given parenterally or orally to relieve inflammation or itching, such as corticosteroids, antihistamines, and injectable immunomodulators, are discussed more extensively in other chapters.

Topical skin preparations can be classified into ten main categories according to their action:

1. *Antipruritics* relieve itching.
2. *Corticosteroids* treat dermatological disorders associated with allergic reactions.
3. *Emollients* and *protectants* soothe the irritation.
4. *Keratolytic agents* loosen epithelial scales.
5. *Enzymatic agents* promote the removal of necrotic or fibrous tissue.
6. *Scabicides* and *pediculicides* treat scabies or lice.
7. Local *anti-infectives* prevent and treat fungal, bacterial, and viral infections.
8. *Burn medications* prevent or treat infections.
9. Specific agents treat acne.
10. *Immunomodulators* reduce the inflammatory response of the immune system.

Factors that influence the rate of absorption of topical medication include condition and location of the skin, heat, moisture, and type of topical formulation in use. If the skin is thick and callused, absorption will be slower. If the skin is moist, macerated (raw), or warm, absorption will be more rapid. Sometimes, the physician will order that the skin be premoistened or a plastic wrap be applied over the ointment to aid absorption; in other cases, the skin must be left exposed to the air to slow absorption and reduce systemic effects. Often, the duration of time for the medication to remain on the skin is very important. The type of topical formulation being used also effects absorption. Gels and creams are more water-based and are absorbed by the skin more quickly, while ointments and pastes are more oil-based and take longer to absorb. Complete understanding of appropriate directions for each topical medication is vital before administration.

Antipruritics

Antipruritics are used short term to relieve discomfort from dermatitis (rashes) associated with allergic reactions, poison ivy, hives, and insect bites. They relieve itching with the use of products, singly or in combination, containing:

- Local anesthetics (e.g., the "-caines," such as benzocaine, dibucaine)
- Drying agents (e.g., calamine)
- Anti-inflammatory agents (e.g., corticosteroids) applied locally or given PO for systemic effect; use should be avoided in patients with pruritus that is not accompanied by inflammation; topical agents are preferred because of fewer adverse effects

- Antihistamines applied locally or given PO for systemic effect (antihistamines applied topically can cause hypersensitivity reactions—use only a few days)

Side effects of antipruritics can include:

Stinging and a burning sensation

❗ Allergic reactions (especially with the "-caines")

Cautions or contraindications for antipruritics include:

Delayed healing—on open wounds for corticosteroids

Prolonged use (especially corticosteroids)

Hypersensitivity (severe allergic) reaction to the active drug or any component of the formulation

Figure 12-1 shows contact dermatitis conditions where antipruritics would be indicated.

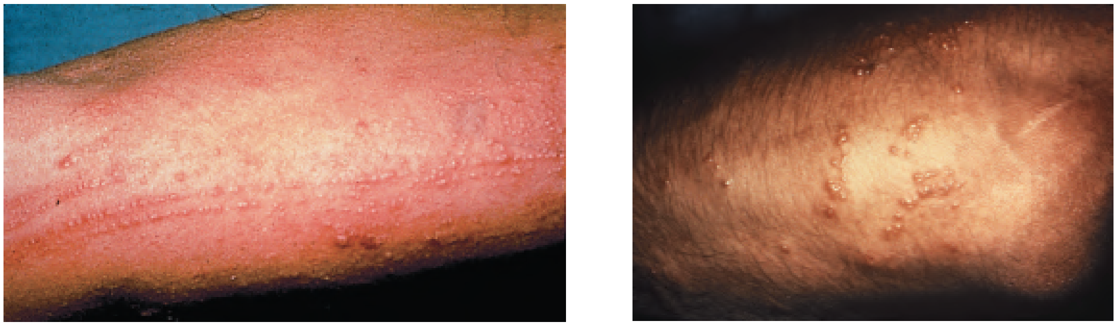

(A)
(B)

Figure 12-1 (A) Allergic contact dermatitis and (B) poison ivy with fluid-filled vesicles. Courtesy of the Centers for Disease Control and Prevention/Richard S. Hibbits.

Patient Education

Patients being treated with antipruritics should be instructed to:

Clean the affected area thoroughly before application

Rub in gently until the medication vanishes

Avoid bringing the medication into contact with eyes or mucous membranes

Avoid covering the area with dressings unless directed by the physician

Avoid prolonged use (not longer than one week)

Discontinue if condition worsens or irritation develops

Trim children's fingernails to reduce the possibility of infection from scratching

Corticosteroids

The corticosteroids are used *both topically and systemically* to treat dermatological disorders associated with allergic reactions. Most topical steroids are available in a variety of dosage forms and potencies (low, medium, high, and very high); the choice depends upon the area affected and the condition being treated. Topical corticosteroids are also used to treat psoriasis and seborrheic dermatitis.

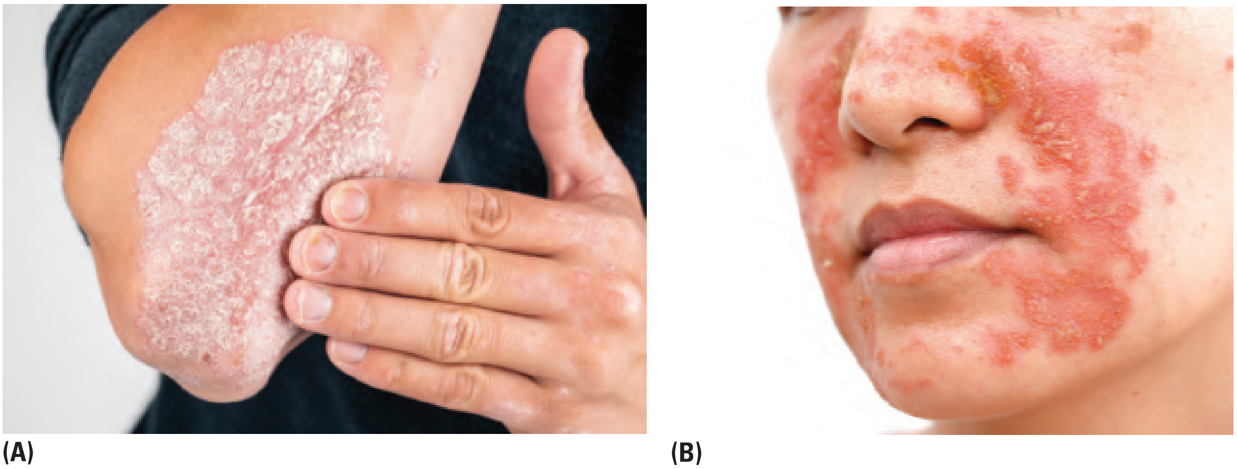
Side effects of corticosteroid ointments and creams, especially used long term (e.g., with psoriasis), can include:

- ❗ Epidermal thinning, with frequent skin tears, increased risk of infection, and frequent bruising
- ❗ Increased fragility of cutaneous blood vessels
- Ulceration, especially with occlusive dressings
- ❗ Activation of latent infections and slow healing

Cautions or contraindications for corticosteroids include:

- Open wounds

Figures 12-2A and 12-2B show psoriasis and seborrheic dermatitis conditions where topical corticosteroids would be indicated.


Fuss Sergey/Shutterstock.com.

(A)

Warut Chinsai/Shutterstock.com.

(B)

Figure 12-2 (A) Psoriasis, a chronic skin disorder with red papules; covered with silvery scales. (B) Seborrheic dermatitis of the face showing crusting over of a red scaly, itchy rash (seborrhea) of the face.

Emollients and Protectants

Emollients and **protectants** are used topically to soothe, soften, protect, and seal out wetness in minor dermatological conditions such as diaper rash, irritation, abrasions, and minor burns. Their purpose is to moisten the skin; this is achieved by utilizing a lipid barrier that does not let moisture out of the skin. In many cases, emollients are used as first-line therapy in eczema and other conditions, which helps to avoid the need for corticosteroid or other medication use. A classic example of an emollient is Balmex, which is used to treat diaper rash.

Keratolytics

Keratolytic agents, for example, salicylic acid, are used to control conditions of abnormal scaling of the skin, such as dandruff, seborrhea, and psoriasis, or to promote peeling of the skin in conditions such as acne, hard corns, calluses, and warts. Antifungals are also used at times for seborrheic dermatitis and dandruff.

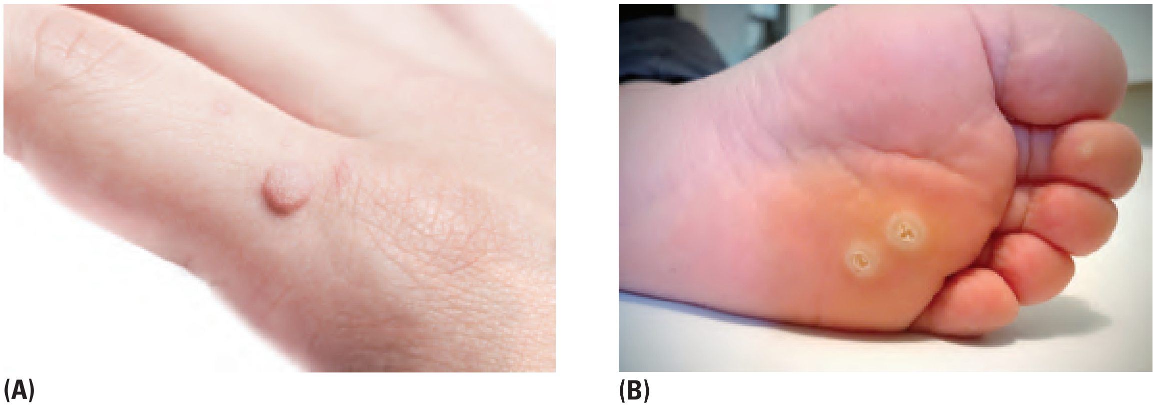
Side effects can include:

- ❗ Irritation to eyes or mucous membranes
- ❗ Photosensitivity

Cautions or contraindications for keratolytics include:

Open areas of the skin

Figures 12-3A and 12-3B show common and plantar warts, conditions where keratolytic agents would be indicated.



LenaProkopenko/Shutterstock.com.

Migren art/Shutterstock.com.

Figure 12-3 (A) Common wart. (B) Plantar wart.

Patient Education

Patients being treated with keratolytics should be instructed to:

- Use only as directed, and for the entire treatment period, even if the condition improves, but not for longer than prescribed
- Avoid contact with eyes and mucous membranes
- Discontinue and seek medical aid if irritation occurs
- Avoid contact with surrounding tissues when applying to warts, corns, or calluses

Enzyme Preparations

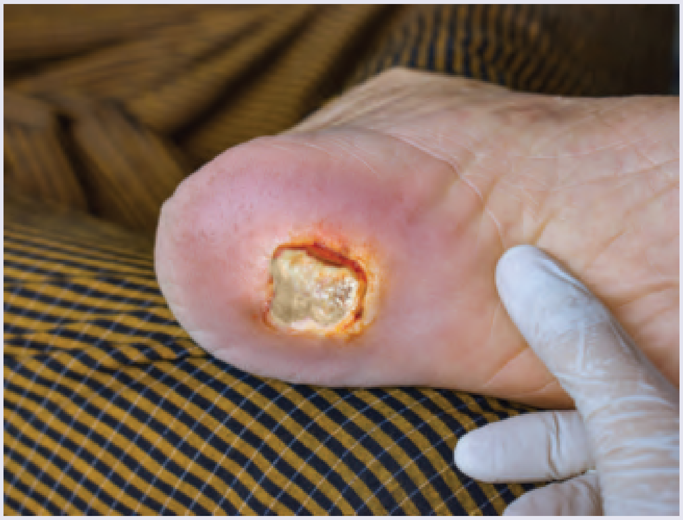
Nonambulatory patients who spend the majority of their time in bed are prone to decubitus ulcers (pressure sores), and patients with diabetes are prone to developing foot ulcers. These ulcerations produce necrotic (dead) skin that must be removed to promote proper healing. Collagenase (Santyl) is a topical enzyme ointment used for the chemical debridement (removal of dead or damaged tissue) of dermal ulcers and burns. Collagenase should be used only on wounds associated with necrotic material. If a topical antibiotic is to be applied to an infected site, the antibiotic is applied before collagenase. Avoid using detergents, povidone–iodine, and heavy metal (e.g., mercury, silver)–containing agents, which will inhibit the enzymatic activity of collagenase.

Refer to Table 12-1 for antipruritics, emollients and protectants, keratolytics, and enzyme preparations.

Clinical Application

Diabetic foot ulcers are common in patients with diabetes. In fact, approximately 15% of all patients with diabetes will experience a foot ulcer at some point. Diabetic foot ulcers are dangerous because many patients with diabetes have decreased sensation in their extremities (from nerve damage), which means they often do not feel the sore until it is already too late. When foot ulcers progress untreated, the infection can lead to limb amputation or even death.

Foot ulcers are treated with antibiotics, enzyme preparations, and sometimes a physician debriding the area of necrotic tissue. The best course of action is prevention. All patients with diabetes should regularly have someone check their feet for developing sores; if needed, they should also wear shoes designed for persons with diabetes that help reduce the risk of foot ulcers.



Zay Nyi Nyi/Shutterstock.com

Table 12-1 Topical Medications for the Skin: Antipruritics, Emollients and Protectants, Keratolytics, and Enzymatics

Generic Name	Trade Name	Available As	Comments
Antipruritics			
Local anesthetics			
benzocaine	Lanacane, Americaine, Orajel	Ointment, spray, gel, lotion, cream, liquid, lozenge	Can cause hypersensitivity reaction
dibucaine	Nupercainal	Ointment	Potential for hypersensitivity

Generic Name	Trade Name	Available As	Comments
lidocaine	Lidoderm	5% patches (may be cut into smaller sizes and can use up to 3 at once)	For post-herpetic neuralgia (on 12 h/off 12 h)
	Xylocaine AneCream Xolido	Topical jelly/cream 2% – 5%	Use for temporary relief of pain or as a numbing agent prior to minor procedures
Antihistamine			
diphenhydramine	Benadryl	Lotion, cream, gel, spray	Not as effective as oral
Corticosteroids			
Very high potency betamethasone	Diprolene, Temovate, others	Ointment, cream, lotion, solution, gel, foam, shampoo (formulations available in all potencies)	Duration is maximum two to four weeks—do not discontinue abruptly if used for a long period of time; avoid occlusive dressings
Various other potencies (high, medium, low) hydrocortisone	Cortaid, Topicort, Lidex, Kenalog, Synalar, others	Ointment, cream	Lower potency agents preferred for the face, groin, armpits, skin folds, or treatment of large surface area
Emollients and Protectants			
ammonium lactate	AmLactin, Lac-Hydrin	Cream, lotion	Moistening, rehydrating agent; also used in sunscreen products
vitamins A and D	A & D Ointment Desitin (with zinc oxide)	Ointment Ointment	Moisturizer to treat dry or rough skin
zinc oxide	Balmex	Cream, ointment	Used for diaper rash
Keratolytics			
coal tar	Balnetar, Polytar, Neutrogena T/Gel	Shampoo, oil, cream, lotion, ointment, soap, solution	For dandruff, seborrheic dermatitis, or psoriasis (stains clothing)
salicylic acid	Clearasil, Fostex, Compound W	Cream, liquid, gel, patches	For dandruff, psoriasis, acne, warts, corns, calluses
sulfur	Many combinations with other keratolytics	Cream, lotion, soap, gel, solution, pads	For acne, scabies, seborrheic dermatitis
Enzyme Preparations			
collagenase	Santyl	Ointment	For use only on necrotic skin tissue

Note: This table lists only typical medications and does not include all of those on the market.

Scabicides and Pediculicides

Scabies is caused by an itch mite that burrows under the skin. Pediculosis is caused by infestation of lice on the hairs of the scalp, pubic area, and trunk. Both are easily transmitted from one person to another by direct contact or through contact with contaminated clothing or bed linens. Effective treatment includes laundering in hot water or dry cleaning all clothing and bedding. Sometimes concurrent treatment of close contacts is recommended.

Scabicides (permethrin 5% or lindane lotion) must be applied *according to directions* on the package insert, left in place the required period of time (usually 8–14 h), and then rinsed thoroughly. Malathion 0.5% lotion is used if permethrin is ineffective. One application is generally curative, although some experts recommend two applications, with the second one separated from the first by one or two weeks. This second application serves to eliminate any remaining scabies, or any that were retransmitted from linens that were missed or not thoroughly washed.

Pediculicides (for example, permethrin 1% and lindane shampoo), are used in the topical treatment of lice infestations. Pyrethrins (e.g., RID shampoo) are considered safer for pediculosis, although a repeat treatment after 7–10 days is needed.

Side effects, rare when applied topically according to directions, may include:

Slight local irritation, rash, or conjunctivitis

Dermatitis with frequent application

However, with excessive or prolonged use, or with oral ingestion or inhalation of vapors, central nervous system (CNS) symptoms and hepatic or renal toxicity may occur. Anemia and seizures have been reported, especially with the use of lindane. Therefore, lindane should be used only in patients who cannot tolerate or have failed first-line treatment for lice with safer medications.

Cautions or contraindications include:

Acutely inflamed, raw, or weeping surfaces

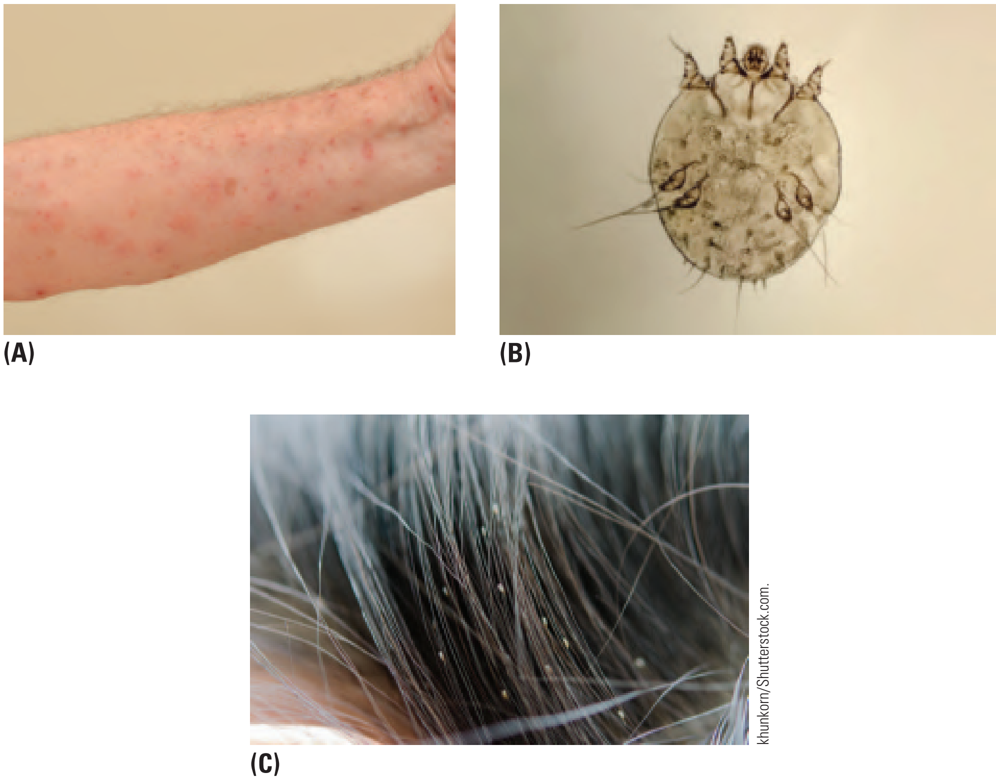
Because lindane can be absorbed systemically following topical application, it should be avoided during pregnancy and lactation, as well as with infants, children, older adults, those who weigh less than 110 pounds, and those with known uncontrolled seizure disorders.

However, permethrin is a safer alternative under these conditions for scabies. Pyrethrins (e.g., RID) are a safer alternative than lindane for pediculosis.

Because of the toxicity of lindane, the oral antiparasitic agent ivermectin (Stromectol) has been used successfully as an alternative (off-label) to treat mass scabies outbreaks in institutional settings and to treat head lice resistant to standard therapies. It is given orally as a single dose (weight-based), with a repeat dose 10–14 days later. The Food and Drug Administration (FDA) approved a topical ivermectin lotion (Sklice) for the treatment of head lice in patients age 6 months or older. The lotion treats lice in most patients with a single 10-minute application to dry hair without nit combing.

People living in close quarters with an individual who has been diagnosed with scabies or lice can be considered for prophylactic therapy. The prophylaxis of scabies consists of two applications of topical malathion, spaced one week apart. For lice, prophylactic treatment is considered for household members and close contacts (especially children who share beds). These people should be treated at the same time with the same medication as the infected person.

Figure 12-4A shows scabies, a condition where scabicides would be indicated, and Figure 12-4B shows the scabies mite. Figure 12-4C shows lice infestations, a condition where pediculicides would be indicated.



Chuck Wagner/Shutterstock.com.

Aliaksei Marozau/Shutterstock.com.

khunkorn/Shutterstock.com.

Figure 12-4 (A) Scabies skin infection (B) and the scabies mite. (C) Lice infestation of the hair.

Patient Education

Patients being treated with scabicides or pediculicides should be instructed to:

- Follow directions carefully (read and understand the medication guide dispensed with the lindane prescription); itching may still occur after the lice have been successfully killed and is not necessarily an indication for retreatment with lindane shampoo
- Thoroughly launder (130°F) clothing and bedding and dry using the hot cycle of a dryer for at least 20 min

Large items (e.g., pillows, comforters) may be bagged in plastic for two weeks

Use caution to prevent accidental oral ingestion

Use caution with infants, who might suck their thumbs

Inform sexual partner if the condition is present in the pubic area

Alert the school if head lice infestation occurs

Local Anti-Infectives

Local anti-infectives are used to treat diseases caused by microorganisms. These diseases include fungal, viral, and bacterial diseases of the skin.

Antifungals

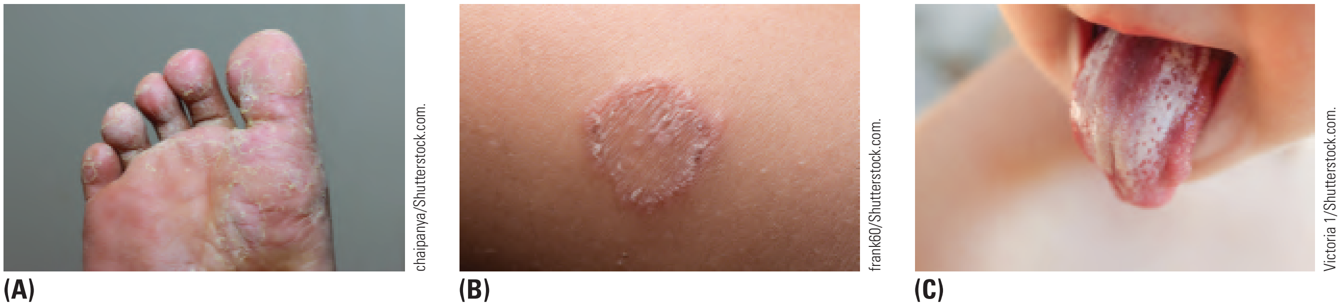
Antifungals, for example, nystatin, are useful in the treatment of fungal infections (candidiasis) such as thrush, diaper rash, and vaginitis. Other antifungals such as clotrimazole (Lotrimin) are used to treat fungal infections such as athlete's foot, body ringworm, and jock itch. Antifungals are also combined with corticosteroids, for example, Lotrisone (betamethasone/clotrimazole) and Mycolog II (nystatin/triamcinolone).

Effective treatment includes topical administration according to directions on the package insert and good hygiene practices, including washing, drying, and exposing to air when possible.

For the treatment of candidiasis of the oral cavity, a nystatin oral suspension administered 4 times daily or clotrimazole oral lozenges administered 5 times daily for 14 days are equally effective. Additionally, fluconazole oral tablets can be used, which would be dosed at 200 mg on the first day and then 100 mg daily for 2 weeks. For infants, administer after the feeding, which is followed by water to rinse the mouth *before therapy*. Place one-half dose in each side of the mouth. For adults, apply *after meals* and *after rinsing* of the mouth. Then the entire dose should be used to thoroughly coat inside the mouth, holding it for as long as possible (e.g., several minutes) before swallowing. In both cases, the patient should be NPO (nothing by mouth) for at least 1 h after treatment. Side effects are rare with topical antifungals.

Contraindication or caution applies to the use of vaginal preparations during pregnancy. Use these preparations only under medical supervision. Some products can cause fetal abnormalities.

Figure 12-5 shows various fungal infections where antifungals would be indicated.


chaipanya/Shutterstock.com.

frank60/Shutterstock.com.

Victoria 1/Shutterstock.com.

Figure 12-5 (A) Athlete's foot; medically known as tinea pedis. (B) Body ringworm; medically known as tinea corporis. (C) Thrush (yeast infection) of the tongue; medically known as candidiasis.

Patient Education

Patients being treated with antifungals should be instructed to:

- Carefully wash *and dry* affected areas
- Expose the affected areas to air whenever possible
- With genital fungus, avoid tight undergarments, pantyhose, and wet bathing suits
- With athlete's foot, use open sandals instead of sneakers
- *Follow application instructions carefully*; use for the entire time, even if asymptomatic
- Remove any stains with soap and warm water
- Continue prescribed vaginal treatment even during menstruation, or if symptomatic relief occurs, until the entire regimen is completed
- Consult a physician before vaginal preparations are used during pregnancy
- For vaginal infections, refrain from intercourse until treatment is complete
- Consider treating partner if reinfection occurs

Antivirals

Acyclovir has an **antiviral** effect on herpes simplex (cold sores or genital herpes), herpes zoster (shingles), and varicella zoster (chickenpox) viruses. Acyclovir (Zovirax) is available in oral and parenteral preparations or is applied topically. Zovirax *cream* is indicated *only* for the treatment of cold sores. Topical therapy is substantially less effective than systemic therapy (parenteral or oral). Topical acyclovir therapy is *not a cure* and does not reduce the frequency or delay the appearance of new lesions. However, topical therapy generally decreases the duration of viral shedding, the duration of pain and itching, and the time required for crusting and healing of lesions. It is effective in first-episode genital herpes infection, but recurrent infections have shown little, if any, therapeutic benefit from topical therapy. The ointment should be applied as soon as possible following the onset of signs and symptoms of infections. Take care not to get the ointment in the eyes. It is *not effective in preventing infections*.

For more effective treatment of herpes zoster (shingles), acyclovir (Zovirax) is available orally. Valacyclovir (Valtrex) and famciclovir (Famvir) are derivatives of acyclovir and can be dosed less frequently, improving patient compliance. *All oral antivirals need to be started within 72 h of rash onset and are most effective if started within the first 48 h of onset.* If antivirals are not effective, or if the time frame for their effective use has passed, other oral medications can be used to treat the pain associated with the shingles rash. These range from anti-inflammatories such as prednisone, dexamethasone, and ibuprofen to opioids such as Percocet and tramadol, and even medications that treat nerve pain such as Lyrica and gabapentin.

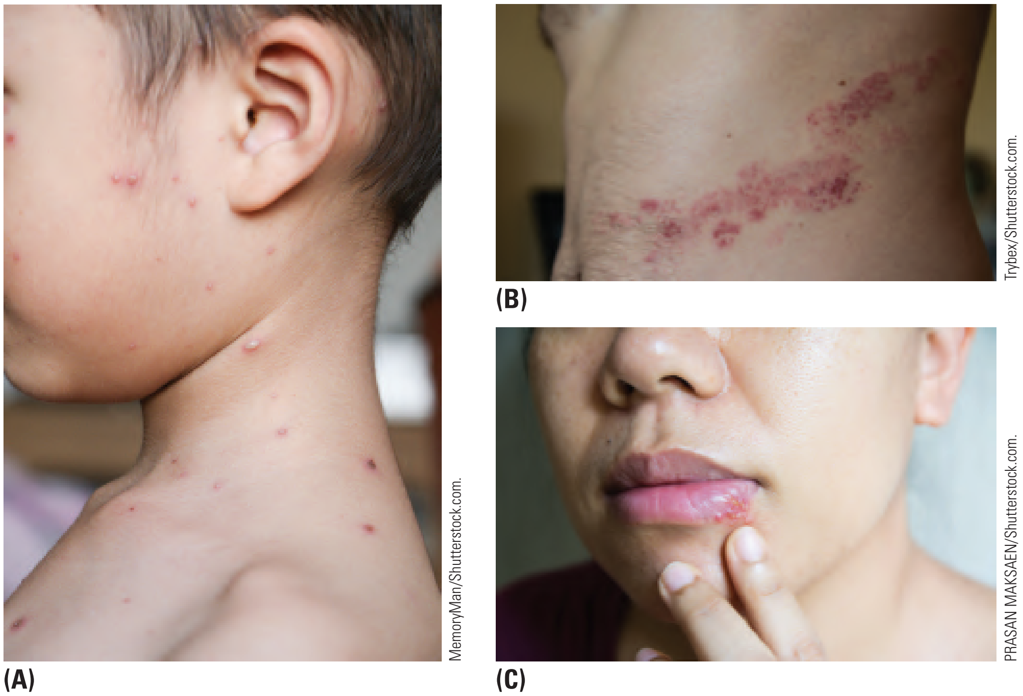
Docosanol (Abreva) is the only over-the-counter (OTC) medication approved by the FDA to shorten the healing time and duration of cold sore symptoms. It helps protect against the herpes simplex virus by modifying the cell membrane, making it difficult for the virus to combine with and penetrate the cell. Apply docosanol as soon as the first symptoms (tingling, redness, bump, or itch) appear.

Figure 12-6 shows various viral skin infections where antivirals would be indicated.

Clinical Application

Patient Education for Shingles

Shingles is a disease that is frequently misunderstood by patients. It is often believed that shingles rash can occur only once in a person's lifetime. This is not true. Therefore, it is important to educate patients who have had shingles that they are still at risk (and possibly greater risk) to develop the rash again. With this information, patients will be more likely to get the Shingrix (shingles) vaccine. The Shingrix vaccine is a two-dose series given two to six months apart. It is recommended for all patients over 50 years old and, depending on age of the individual, has been shown to be 91–97% effective at preventing an occurrence of the shingles rash. Some patients may think that they do not need Shingrix since they have already had an older shingles vaccine called Zostavax. Zostavax had 70% effectiveness in comparison and is no longer commercially available. Patients who had Zostavax should still receive the Shingrix vaccine. Additionally, Shingrix is not a live vaccine like Zostavax, so patients who could not receive Zostavax for that reason can be immunized with Shingrix. Many patients believe that if they did not have (or do not remember having) the chickenpox, they are not at risk of developing the shingles rash. Again, this is not true. Even in the unlikely case that they have not been exposed, receiving the Shingrix vaccine is still recommended and safe.


MemoryMan/Shutterstock.com.

Trybex/Shutterstock.com.

PRASAN MAKSAEN/Shutterstock.com.

Figure 12-6 (A) Chickenpox caused by varicella zoster. (B) Shingles, a later eruption of the chickenpox virus as the herpes zoster virus. Note the characteristic "band" shape of the rash around the rib and trunk area. (C) Cold sores of the mouth caused by herpes simplex virus.

Antibacterial Agents

Mupirocin (Bactroban) is an antibiotic that is structurally unrelated to any other topical or systemic antibiotics. Mupirocin ointment is used topically to treat impetigo caused by *Staphylococcus aureus* and certain species of *Streptococci*. The ointment is used to treat secondarily infected traumatic skin lesions. Mupirocin nasal ointment is applied intranasally to reduce the risk of infection in patients with high risk during institutional outbreaks of MRSA (methicillin-resistant strains of *S. aureus*).

There are many other prescription and OTC topical antibacterial agents on the market, including ointments, creams, and solutions too numerous to mention here. These products have the potential for adverse side effects, including local, hypersensitivity, and systemic reactions. Overuse or extended use of antibacterial agents can also lead to *resistance*.

Figure 12-7 shows an impetigo infection, a condition where an antibacterial agent would be indicated.

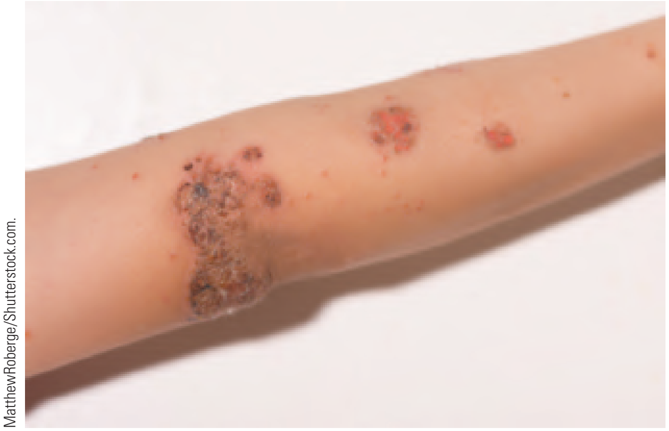

MatthewRoberge/Shutterstock.com.

Figure 12-7 Impetigo is a highly contagious bacterial skin infection commonly found in children.

Patient Education

Patients using any topical antibacterial agent should be instructed to:

- Read and carefully follow all directions on the package
- Check all ingredients carefully for possible allergies
- If there is no improvement, the condition worsens, or there are other adverse reactions (e.g., inflammation, itching, rash, or swelling), stop the medication and consult a physician

Antiseptics

Antiseptics are substances that inhibit the growth of bacteria (bacteriostatic). The term is used most frequently to describe chemicals applied to body tissues, especially the skin. *Disinfectants* are included in this category, but chemicals that kill bacteria (**bactericidal**) are frequently too strong to be applied to body tissues and are *usually* applied to inanimate objects, such as furniture, floors, and instruments. Sometimes a chemical can be used as an antiseptic on skin and also as a disinfectant on inanimate objects by increasing the strength.

The two major antiseptics in use today are chlorhexidine and povidone–iodine, used for surgical scrubs and as bacteriostatic skin cleansers. Prior to surgery, skin cleansing with chlorhexidine is preferred because of lower rates of surgical site infections compared to povidone–iodine. Some iodine preparations are also bactericidal and are used to treat superficial skin wounds and to disinfect the skin preoperatively. Chlorhexidine (Hibiclens) should not be used on wounds involving more than the superficial layers of the skin. It is important to rinse thoroughly after use.

Side effects of chlorhexidine can include:

- ❗ Dermatitis and irritation
- Photosensitivity (increased reaction such as burning from brief sun exposure)
- ❗ Allergic reactions, especially in the genital area

Side effects of povidone–iodine (Betadine) can include:

- ❗ Skin irritation or burns
- ❗ Allergic reactions in all areas of the body

Cautions or contraindications for chlorhexidine include:

- Pregnancy category B
- Not for frequent use for total body bathing
- Not for use in eyes and ears

Cautions or contraindications for povidone–iodine include:

- Not for use in those allergic to iodine
- Not for use on open wounds
- Not for use in newborns (risk of iodine absorption)

Refer to Table 12-2 for a summary of scabicides, pediculicides, antifungals, antivirals, antibacterials, and antiseptics.

Patient Education

Patients being treated with local anti-infectives should be instructed to:

- Rinse chlorhexidine *thoroughly*
- Avoid chlorhexidine for frequent use
- Avoid use of chlorhexidine on open skin lesions, mucous membranes, and genital areas
- Take care to avoid chlorhexidine or povidone–iodine in the eyes or ears; flush thoroughly
- Use caution with povidone–iodine in anyone with allergies

Table 12-2 Medications for the Skin: Scabicides, Pediculicides, Antifungals, Antivirals, Antibacterials, and Antiseptics

Generic Name	Trade Name	Available as	Comments
Scabicides and Pediculicides			
permethrin	Acticin, Elimite	5% cream (Rx)	Apply from head to feet, wash off after 8–14 h
		1% lotion (OTC)	Apply to damp hair, to remain on for 10 min
malathion	Derbac M	0.5% lotion	Apply to the hair and scalp one time. Treatment may be repeated after 7 to 9 days, if necessary.
lindane	Argocide	Lotion, shampoo	Second-line therapy due to toxic potential
pyrethrins	RID	Shampoo	For head lice only
ivermectin	Stomectol	3-mg tabs	For scabies/head lice
	Sklice	0.5% lotion	10-min application to dry hair
ANTI-INFECTIVES			
Antifungals[a]			
clotrimazole	(Mycelex)[b] Lotrimin Gyne-Lotrimin	Troches, cream, lotion, sol, vaginal cream	For oral, topical, or vaginal application
ketoconazole	Nizoral	Cream, 2% shampoo (Rx)	Topical antifungal, shampoo for dandruff
	Nizoral A-D	1% shampoo (OTC)	
miconazole	Monistat Lotrimin AF	Cream, gel, ointment Powder, spray	Also vaginal cream and suppositories
nystatin	(Mycostatin)[b]	Oral suspension, tabs, cream, ointment, vaginal tab, powder	Apply oral suspension or lozenges PC, then NPO 1 h
terbinafine	Lamisil AT Lamisil (Rx)	Cream, gel, spray tabs, granules	Oral form very effective for nail infections (onychomycosis)
tolnaftate	Tinactin	Aerosol spray, cream, powder, solution	Avoid inhaling spray or powder contact with eyes

Generic Name	Trade Name	Available as	Comments
Antivirals			
acyclovir	Zovirax	Cream	For cold sores only: 5 times per day for 4 days
		Ointment, orally[a]	6 times per day (q3h) for 7 days
penciclovir	Denavir	Cream	q2h while awake for cold sores
docosanol	Abreva	Cream	5 times per day for 10 days max; wash hands before/after
Antibacterials			
metronidazole	MetroCream MetroGel MetroLotion	Cream Gel Lotion	Rosacea
mupirocin	Bactroban	2% cream, ointment	Avoid contact with eyes
neomycin/polymixin B/ bacitracin	Neosporin Triple Antibiotic	Ointment Cream	Prevents infection in minor scrapes and cuts
Antiseptics			
chlorhexidine	Hibiclens	Solution, liquid, foam	Antimicrobial skin cleanser, surgical scrub; rinse thoroughly
	Peridex	Oral rinse for Tx of gingivitis	
povidone–iodine	Betadine	Aqueous solution, ointment, liquid scrub, spray	Bactericidal, antiseptic, surgical scrub; watch for allergies

[a] Oral preparations and dosing are discussed in Chapter 25.

[b] Brand name is no longer marketed, but the name is still commonly used.

Note: Other preparations are available. This is a representative list.

Burn Medications

Burns are injuries to the skin and tissues below the skin that are caused by heat from flames, hot liquids, steam, heated objects, chemicals, friction, electricity, radiation, or the sun. They are usually classified as first-degree (superficial), second-degree (partial-thickness), or third-degree (full-thickness) burns, depending upon their severity and the depth to which tissues have been damaged (Figure 12-8).

Burn treatments include topical application of medications to prevent or treat infections associated with the damaged skin. The two most commonly used agents for this purpose in second- and third-degree burns are silver sulfadiazine (Silvadene) and mafenide (Sulfamylon). These agents should be applied with a sterile-gloved hand.

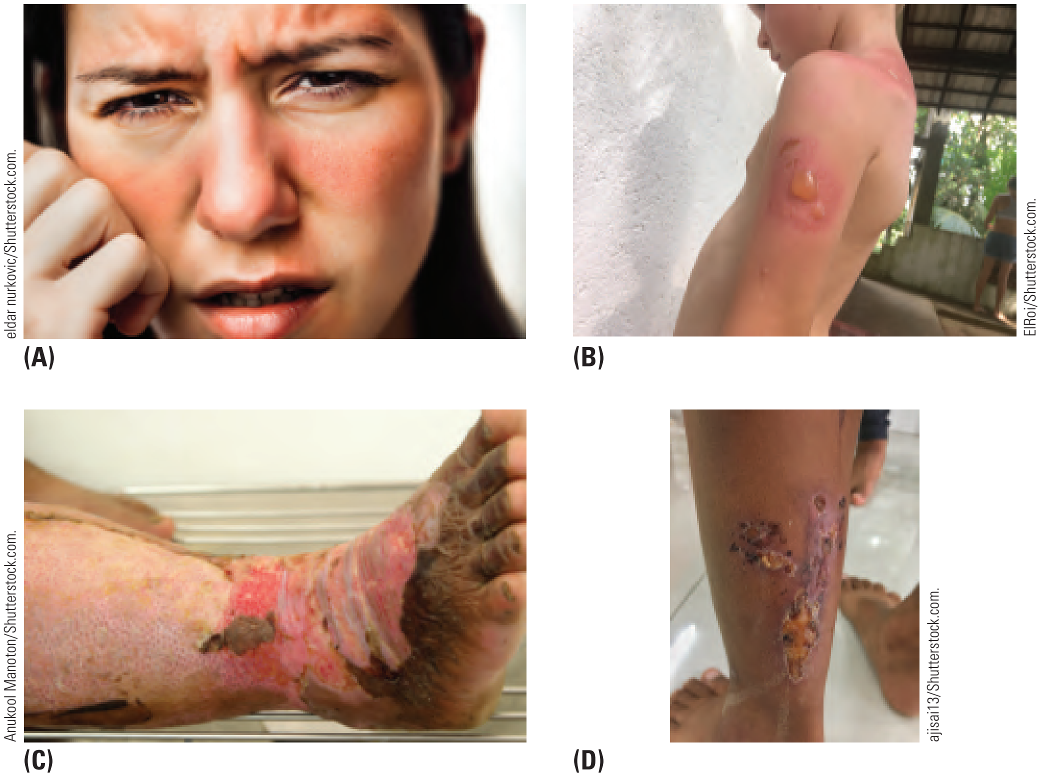
Side effects of burn medications can include:

❗ Pain, burning, and itching

Staining of the skin temporarily

Cautions or contraindications apply to newborns or to patients with:

- Impaired kidney or liver function (cumulative effects)
- History of allergy, especially to sulfa drugs



eldar nurkovic/Shutterstock.com.

ElRoi/Shutterstock.com.

Anukool Manoton/Shutterstock.com.

ajisai13/Shutterstock.com.

Figure 12-8 Examples of varying degrees of burns. (A) First-degree, superficial. (B) Second-degree, partial thickness. (C) Third-degree, full thickness. (D) Third-degree, full thickness.

Patient Education

Patients using burn medications should be instructed to:

- Use aseptic technique to prevent infection
- Watch for allergic reactions
- Keep careful intake and output records
- Keep the affected area covered at all times with cream and sterile dressing

Sunscreens

Nearly every person has experienced the pain of sunburn at some point. Overexposure to the sun is considered to be the primary cause of skin cancer, which is the most common form of all cancers in the United States, with more than 5 million new cases diagnosed each year. Ultraviolet (UV) radiation is a type of invisible light emitted by the sun and can be divided into two types: UVA and UVB.

Sun protection factor (SPF) is a measure of the protection a sunscreen offers. Only broad-spectrum sunscreens (both UVA and UVB) with an SPF value ≥30 can claim to reduce the risk of skin cancer and early skin aging if used as directed with other skin protection measures. Those measures include applying sunscreen to dry skin at least 15 to 30 min prior to sun exposure, limiting sun exposure (especially between 10 A.M. and 4 P.M.), wearing sun-protective clothing, using water-resistant sunscreens when swimming or sweating, and reapplying at least every 2 h (even on cloudy days).

Agents Used to Treat Acne

Acne is a common condition of the skin that affects almost everyone to some degree during adolescence and some people even into adulthood. Acne is most commonly seen on the face, scalp, neck, chest, back, and shoulders.

Patients with mild acne may choose from several *nonprescription topical* medications such as sulfur, salicylic acid, and benzoyl peroxide. A patient with more severe disease or who desires treatment from a dermatologist may be prescribed topical therapy with a combination of a retinoid (e.g., isotretinoin—decreases oil production) and *topical antibiotics* (e.g., clindamycin or erythromycin—decrease inflammation). For more severe forms of acne, a course of *oral antibiotics* (tetracyclines or erythromycin) may be prescribed in addition to topical products. For patients who produce too much testosterone, *systemic estrogen and progestin hormones* (*birth control pills*) may be of benefit. Retinoids taken by mouth (e.g., isotretinoin) are used for the most severe forms of acne and for patients who fail other treatments. (The *Isotretinoin Medication Guide* produced by the drug manufacturer describes treatment with cautions regarding possible severe side effects.) Patients on Claravis and generic isotretinoin are monitored via the iPLEDGE program since use during pregnancy has been linked to birth deformities. Each month patients must verify with the prescribing physician that they are not pregnant and are using birth control if sexually active before the physician can sign off and the pharmacy can fill the prescription.

Side effects of benzoyl peroxide can include:

❗ Skin irritation, mild stinging, redness, dry skin

Cautions for benzoyl peroxide include:

❗ Contraindicated with pregnancy and breastfeeding

Use in patients with skin diseases (dermatitis, eczema, sunburn, etc.) may increase the risk of skin irritation

Benzoic acid or paraben hypersensitivity

Avoid exposure to the eyes or mucous membranes; can cause severe irritation

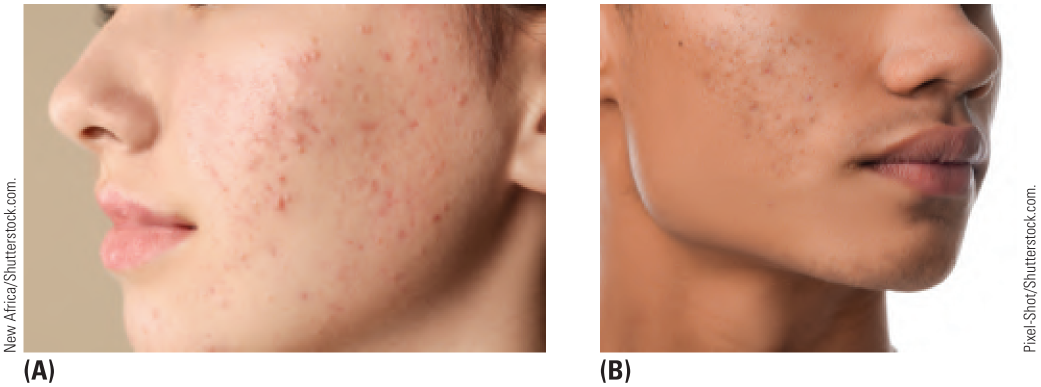
Refer to Table 12-3 for burn medications and acne medications.

Figure 12-9 shows the skin condition of acne.

Table 12-3 Medications for the Skin: Burn Medications, Acne Medications, and Topical Immunomodulators

Generic Name	Brand Name	Available as	Comments
Burn Medications			
silver sulfadiazine	Silvadene, SSD	Cream	Watch for sulfa allergies
mafenide	Sulfamylon	Cream, powder for solution	Use with caution in sulfa-allergic patients
Acne Medications			
benzoyl peroxide	Panoxyl, others	Bar, cream, gel, liquid, lotion, foam	Antibacterial activity Drying actions, for type 1 acne
dapsone	Aczone	Gel	Daily for acne vulgaris
isotretinoin	Claravis	10-, 20-, 30-, 40-mg caps	Absolutely contraindicated in pregnancy, for type 4 acne
salicylic acid	Clearasil, Neutrogena	Cream, liquid, gel, pads	Mild acne
sulfur	Many combinations with other keratolytics	Cream, lotion, gel, pads, soap	Mild acne
tretinoin	Retin-A	Cream, gel	Increases sensitivity to the sun
Topical Immunomodulators			
tacrolimus	Protopic	Ointment	Approved for severe atopic dermatitis
pimecrolimus	Elidel	Cream	Approved for moderate atopic dermatitis
crisaborole	Eucrisa	Ointment	Side effects of burning and stinging decrease with time
ruxolitinib	Opzelura	Cream	Black Box Warning: may increase the risk for serious infections, cancer, blood clots, heart attack, or stroke

Note: Other preparations are available. This is a representative list.


(A) (B)

New Africa/Shutterstock.com.

Pixel-Shot/Shutterstock.com.

Figure 12-9 (A) Acne papules and nodules and (B) acne scarring.

Topical Immunomodulators

Newer therapies have been and continue to be developed to treat skin conditions; some of these therapies work by reducing the immune system's inflammatory response. Many skin conditions are caused or worsened by an overactive immune response, and decreasing this can provide relief from itching, redness, and discomfort. Systemic immunomodulators are widely available and can be administered orally or by injection. The benefit to topical application is that the medication acts locally and does not affect the entire body as much as other applications do. Topical immunomodulators are used to treat many skin disorders, including psoriasis and severe persistent atopic dermatitis.

Calcineurin Inhibitors such as tacrolimus (Protopic ointment) and pimecrolimus (Elidel cream) prevent immune cells from reacting to allergens and irritants. PDE4 Inhibitors such as crisaborole (Eucrisa ointment) work by blocking enzymes in the skin cell’s inflammatory pathway. JAK Inhibitors such as ruxolitinib (Opzelura cream) block chemical signals that are involved in promoting inflammation.

Side effects of topical immunomodulators include:

- Burning, stinging, redness, or itching
- Tingling skin
- Change in skin color
- Photosensitivity

Cautions for topical immunomodulators include:

- Pregnancy or breastfeeding
- Active viral infection such as varicella or herpes (zoster or simplex)
- Hypersensitivity to any of the components of the medication

Patient Education

Patients being treated with acne agents should be instructed to:

- Use preparations every day as directed; often these agents take several weeks to be effective (the acne may actually get worse during the first few weeks of treatment, then start to improve)
- Do not use benzoyl peroxide with other topical acne products or retinoids
- Avoid prolonged exposure to sunlight (UV)—use sunscreen and protective clothing; avoid drugs such as sulfas that make you more sensitive to the sun
- Avoid multivitamins or nutritional supplements that contain vitamin A, tetracycline antibiotics, certain antacids (aluminum hydroxide), and certain birth control pills (progestin-only) while taking isotretinoin

Cautions for Topical Medications

Skin medications by prescription or OTC are too numerous to mention. Many patients use products without adequate instruction in administration, side effects, or precautions. The health care professional has a responsibility to advise patients whenever possible to use great caution with self-medication to avoid ineffective or dangerous treatment. Both the health care professional and the layperson should *read instructions completely* before administration of any medication.

Patient Education

Patients using topical medications should be instructed regarding:

- Even though these products are not in a pill form or may not require a prescription (in some cases), this does not mean they cannot cause harm if overused or misused
- *Never* taking by mouth
- Keeping out of reach of children
- Being sure labels are not obscured and are read completely
- Avoiding application to broken skin unless instructed otherwise
- Discontinuing at once with any side effects and seeking medical advice
- Not taking beyond the time limit listed on the medication container
- Avoiding self-medication without medical advice

Case Study A

Skin Medications

A 54-year-old patient noticed patches of irritated skin on elbows, knees, and scalp. During an appointment with a dermatologist, the patient is diagnosed with psoriasis. The physician prescribed a keratolytic agent for treatment of the psoriasis. The patient would benefit from the following information.

1. Keratolytic agents are used to control:
   a. Necrotic tissue
   b. Pruritus
   c. Scaling skin
   d. Fungal infections

2. A common side effect of a keratolytic agent is:
   a. Skin bruising
   b. Skin discoloration
   c. Glycosuria
   d. Severe skin irritation

3. Which instruction should the patient receive about the keratolytic agent for their psoriasis?
   a. Treat irritated skin with the medication as needed.
   b. Avoid contact with the eyes.
   c. Discontinue use if the condition is no longer present or improves, even if midway through treatment.
   d. Use on surrounding tissues to ensure adequate coverage.

4. Which of the following is an example of a keratolytic agent?
   a. Collagenase
   b. benzocaine
   c. salicylic acid
   d. Ammonium lactate

5. Keratolytic agents can also be used to treat:
   a. Allergic contact dermatitis
   b. Fungal infections
   c. Eczema
   d. Warts

Case Study B

Skin Medications

A 64-year-old patient is about to undergo a right total knee replacement. The nurse explains that an antiseptic will be used preoperatively. The patient will find the following information helpful.

1. Antiseptics are substances that perform which of the following actions?
a. They inhibit the growth of bacteria.
b. They assist with the chemical debridement of tissue.
c. They enhance the growth of healthy skin flora.
d. They inhibit the replication of a virus.

2. The most preferred antiseptic for skin cleansing prior to surgery is:
a. Povidone–iodine
b. Terbinafine
c. Mupirocin
d. Chlorhexidine

3. Side effects of chlorhexidine can include:
a. Petechiae
b. Dermatitis
c. Freckling of the skin
d. Whitening of the skin

4. The nurse explains to the patient that they will need to perform the antiseptic scrub at home the night prior to the surgery. The patient should be instructed to:
a. Leave the medication on their skin after application
b. Apply the medication to their eyes and ears
c. Rinse their skin thoroughly after use
d. Apply the medication to all areas involving the dermis

5. The best surgical scrub for a patient with an allergy to iodine is:
a. Peridex
b. Betadine
c. Hibiclens
d. Bactroban

Chapter Review Quiz

Multiple Choice

1. Which of the following is not true regarding the absorption of topical skin medications?

a. If the skin is thick and callused, absorption will be slower.

b. If the skin is moist or warmer than normal, absorption will be faster.

c. If the skin is covered with plastic wrap, absorption will be faster.

d. If an ointment is used instead of a cream, absorption will be faster.

2. Which category of topical skin preparation is used to protect the skin and soothe irritation?

a. Antipruritic
c. Enzymatic agent
b. Keratolytic agent
d. Emollient

3. Oral antiviral medications are most effective if started within how many hours of the onset of symptoms?

a. 72
c. 36
b. 96
d. 48

4. Collagenase (Santyl) would be indicated to treat:

a. Hives
c. Necrotic tissue
b. Scaly skin
d. Psychiatric disorders

5. Which action should a patient take after using a nystatin oral preparation?

a. Spit out the excess.
c. Wipe off the excess.
b. Rinse the mouth.
d. Maintain NPO for at least 1h.

6. Which antipruritic would be most likely to cause a hypersensitivity reaction?

a. Synalar
c. Cortaid
b. benzocaine
d. Desitin

7. Which preparation is used to prevent an infant from developing diaper rash?

a. Keratolytic
c. Enzyme preparation
b. Protectant
d. Antipruritic

8. A patient using a burn medication should be instructed to:

a. Allow the burn to be open to air

b. Disregard any signs of allergy

c. Use the aseptic technique to prevent infection

d. Use an enzymatic debriding agent to facilitate healing

9. Which of the following is an antibacterial cream used topically to treat impetigo?

a. lindane
c. Mycostatin
b. Bactroban
d. Monistat

10. Patients with mild acne would most likely be treated with:

a. Benzoyl peroxide

b. Tetracycline

c. Systemic hormones

d. Isotretinoin

Chapter 13

Autonomic Nervous System Drugs

Key Terms and Concepts

Adrenergic
Alpha-blockers
Anticholinergics
Autonomic
Beta-blockers
Cholinergic drugs

Objectives

Upon completion of this chapter, the learner should be able to:

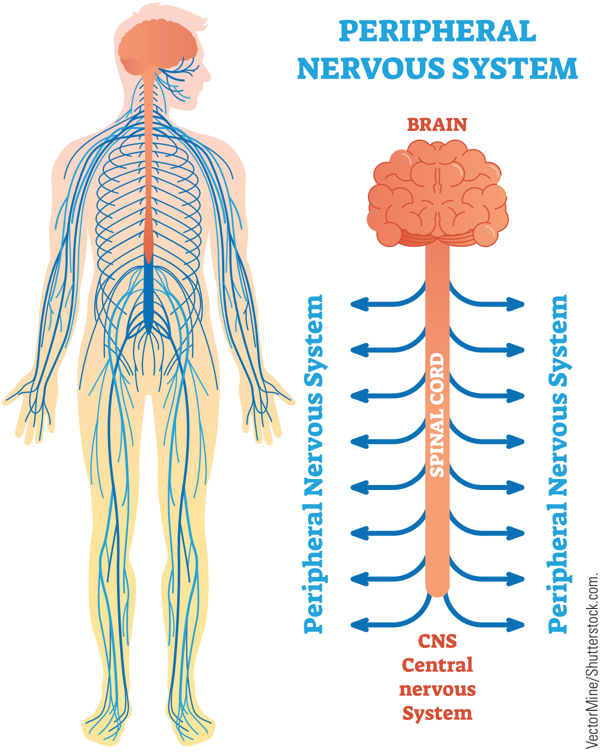
1. Describe the sympathetic and parasympathetic nervous systems.
2. Contrast the four categories of autonomic nervous system medications.
3. List the most frequently used (key) medication in each of the four categories and the purpose of their administration.
4. Describe the possible side effects of each of the key medications.
5. Relate patient education concepts that pertain to the four categories of autonomic nervous system medications.

The autonomic nervous system can be a challenging topic to understand, but it is essential in establishing a foundation to understand medication actions in several system chapters such as the respiratory, cardiovascular, and urinary chapters. These various systems use autonomic drugs to target alpha and beta agonists and blockers to treat diseases such as asthma, blood pressure conditions, other heart conditions, incontinence, and migraine headaches, to name a few. Therefore, a solid understanding of the autonomic nervous system will help you in several upcoming chapters.

The central nervous system (CNS) consists of the brain and spinal cord. The peripheral nervous system (PNS) is comprised of all the nerves that lie outside of the brain and spinal cord (Figure 13-1).

The peripheral nervous system is what connects the rest of your body, neurologically speaking, to your brain and spinal cord. The PNS is broken down into the somatic branch, which consciously controls our skeletal muscles, and the autonomic branch, which unconsciously controls our smooth muscle, cardiac muscle, and glands. Our focus for this chapter is on the autonomic nervous system.

The **autonomic** nervous system (ANS) can be thought of as being *automatic*, self-governing, or involuntary. We have no conscious control over the action of the


PERIPHERAL NERVOUS SYSTEM
BRAIN
Peripheral Nervous System
SPINAL CORD
Peripheral Nervous System
CNS
Central nervous System

VectorMine/Shutterstock.com.

Figure 13-1 The nervous system.

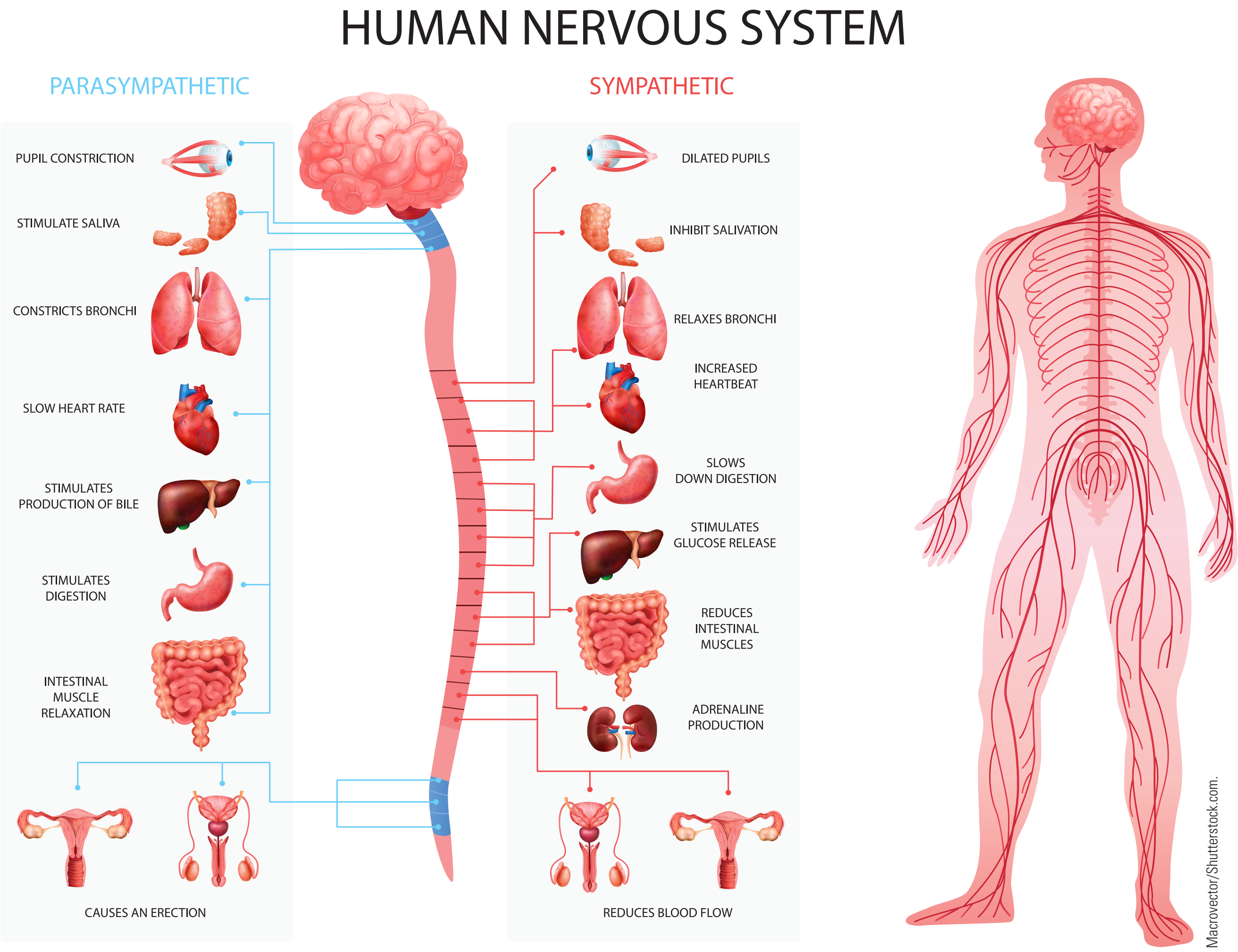
ANS. The autonomic system can further be divided into the sympathetic and parasympathetic nervous systems. The sympathetic system is your “alert system” that can quickly ready your body to face emergencies. The parasympathetic system can be thought of as your “resting and digesting” system and automatically helps to maintain the normal body functions—again, without your conscious effort. Chemical substances called *neurotransmitters* are released at the nerve endings within these systems to transmit the nerve impulses from nerve to nerve at the synapses or from nerve to smooth muscle, cardiac muscle, or glands.

One can try to memorize all the various sympathetic and parasympathetic responses, but a much easier way to truly learn them is through visualization. Visualize yourself jogging along a path and all of a sudden, a large snarling dog baring its teeth runs toward you. Your sympathetic nervous system will immediately kick in to cause physiologic responses to ready you for fight or flight. These responses include pupil dilation to get more light in to see the situation, increased rate and force of contraction of the heart to increase the blood supply, and bronchodilation to enhance ventilation and increase oxygenation. In addition, certain vascular changes would take place to provide more blood flow to essential areas and constrict blood to nonessential areas such as your digestive system. These are all sympathetic responses to get you “up” for the crisis. Drugs that *mimic* these responses would be called sympatho *mimetics*. These drugs are also known as **adrenergic**, and you can think of the adrenalin rush that occurred when you saw that dog.

Now the owner of the dog emerges and leashes the animal, and you begin to calm down. Now the parasympathetic system brings you back down toward homeostasis or resting state by doing the opposite physiologic responses. Your pupils constrict back down to normal, your heart rate slows to normal, and your airways bronchoconstrict to normal tone. These are all parasympathetic responses to bring you back "down" to normal. Drugs that *mimic* these responses are called parasympatho *mimetics*. These drugs are also called cholinergic because acetylcholine (ACh) is the neurotransmitter substance in the parasympathetic system that causes the response. Figure 13-2 contrasts the parasympathetic and sympathetic nervous system physiologic responses. Notice how they work in opposition to balance each other.

While Figure 13-2 illustrates the physiologic responses, these responses can be caused pharmacologically by medications that will either *stimulate* (-mimic) the sympathetic and parasympathetic nervous systems or even *block* (-lytic) the sympathetic and parasympathetic nervous systems. Drugs that affect the function of the ANS are therefore divided into four categories based on whether they mimic or block the response of the sympathetic and parasympathetic nervous systems:

1. Adrenergics (sympathomimetics = mimic sympathetic responses)
2. Adrenergic blockers (sympatholytic = block sympathetic responses)
3. Cholinergics (parasympathomimetics = mimic parasympathetic responses)
4. Cholinergic blockers (parasympatholytics = block parasympathetic responses)


HUMAN NERVOUS SYSTEM
PARASYMPATHETIC
PUPIL CONSTRICTION
STIMULATE SALIVA
CONSTRICTS BRONCHI
SLOW HEART RATE
STIMULATES PRODUCTION OF BILE
STIMULATES DIGESTION
INTESTINAL MUSCLE RELAXATION
CAUSES AN ERECTION
SYMPATHETIC
DILATED PUPILS
INHIBIT SALIVATION
RELAXES BRONCHI
INCREASED HEARTBEAT
SLOWS DOWN DIGESTION
STIMULATES GLUCOSE RELEASE
REDUCES INTESTINAL MUSCLES
ADRENALINE PRODUCTION
REDUCES BLOOD FLOW

Macrovector/Shutterstock.com.

Figure 13-2 The autonomic nervous system and responses.

Adrenergics

Again, adrenergics mimic the action of the "fight-or-flight" sympathetic nervous system. Think back to the snarling dog. There were a lot of responses that had to happen simultaneously in different parts of your body. The sympathetic system has several types of adrenergic receptors that cause specific responses. Alpha receptors are found in the blood vessels and when stimulated cause vasoconstriction of the smooth muscle in the blood vessels. This is what is responsible for shifting blood to essential areas and raising your blood pressure. Alpha receptors in the pupils of the eyes cause pupil dilation to increase your vision. Beta$_1$ receptors are found in the heart and when stimulated increase the rate and force of contraction of the heart. Beta$_2$ receptors are found mainly in the lungs and when stimulated cause bronchodilation by relaxing the smooth muscle around the airways. In essence, the beta receptors get your heart going and make it easier to breathe in a terrifying situation. Table 13-1 presents a summary of the types of adrenergic receptors.

Table 13-1 Adrenergic Receptors

Type	Where Found	Response When Stimulated
Alpha	Blood vessels Pupil	Vasoconstriction (reduce blood flow and increase blood pressure) Dilates pupil (this is termed mydriasis)
Beta$_1$	Heart	Increase rate and force of contraction
Beta$_2$	Airways of lungs	Bronchodilate

Note: There are additional adrenergic receptors, but these are the main ones to concern ourselves with for this chapter.

Learning Hint

To keep the beta receptors straight, think that you only have one heart (beta$_1$) and two lungs (beta$_2$). Of course, if you are stimulating these receptors in a sympathetic response such as the snarling dog, you are going to want to "get your heart going" (beta$_1$ adrenergic) and make it easier to breathe by bronchodilation (beta$_2$ adrenergic). Also, to relate the alpha receptors, if you have ever taken a decongestant, either by pill or nasal spray, you have used an alpha-adrenergic drug. The drug targets the blood vessels to vasoconstrict and thus lessen the congestion due to decreased blood flow to that area. A good way to remember this is thinking of the lowercase Greek letter alpha (α). Visually it looks like it is being constricted in the middle, just like the vasoconstriction that occurs in your nasal blood vessels when alpha receptors are stimulated.

The neurotransmitters released at the sympathetic nerve endings are called catecholamines and include norepinephrine and dopamine. In addition, the hormone epinephrine is secreted by the adrenal glands in response to strong sympathetic stimulation. Drugs that mimic the action of the sympathetic nervous system are called sympathomimetic or **adrenergic**.

Actions of the adrenergics include:

- Cardiac stimulation
- Increased skeletal muscle strength
- Peripheral vasoconstriction
- Bronchodilation
- Dilation of the pupils (mydriatic action)

Uses of the adrenergics include:

- Restoring rhythm in cardiac arrest
- Elevating blood pressure in shock
- Constricting capillaries (e.g., applied topically to relieve nosebleed or nasal congestion, or combined with local anesthetics for minor surgery)
- Dilating bronchioles in acute asthmatic attacks, bronchospasm, or anaphylactic reaction
- Ophthalmic procedures

Side effects of the adrenergics may include:

- ❗ Cardiac side effects associated with increased heart rate and blood pressure
- ❗ Nervousness or tremor
- ❗ Hyperglycemia
- Tissue necrosis (when applied to laceration of periphery—e.g., nose, fingers, and toes—because of blood flow restriction; if too much vasoconstriction occurs, the tissues will not receive enough oxygen)
- Headache and insomnia

Cautions/contraindications for adrenergics apply to those with:

- Angina
- Coronary insufficiency
- Hypertension
- Cardiac arrhythmias
- Angle-closure glaucoma
- Hyperthyroidism

Caution for adrenergics also with dose and route of administration; check dosage carefully (small amounts only); give subcutaneous, intramuscular (IM; deltoid), or intravenous (IV)

Interactions of adrenergics may occur with:

- Central nervous system (CNS) drugs (e.g., certain general anesthetics, monoamine oxidase inhibitors [MAOIs], and antidepressants)
- Propranolol (Inderal) or other beta-adrenergic blockers
- Terazosin (Hytrin) or other alpha-adrenergic blockers

Table 13-2 presents a summary of the adrenergics.

Figure 13-3 shows an epinephrine syringe and epinephrine injector for administering epinephrine to treat or prevent anaphylactic shock.

Table 13-2 Representative Adrenergic Medications

Generic Name	Trade Name	Dosage	Comments
epinephrine	Adrenalin	0.1–0.5 mL 1:1,000 sol SQ or IM[a] (deltoid) 5–10 mL 1:10,000 sol IV	For bronchospasm, asthma, cardiac arrest
	EpiPen, EpiPen Jr	0.3 mL (1:1,000 or 1:2,000) IM	anaphylaxis
dopamine		2–5 mcg/kg per min IV initially; titrate to response	To raise blood pressure, cardiotonic
isoproterenol	Isuprel	0.02–0.2 mg IV or IM; 5 mcg/min infusion	For heart block or ventricular arrhythmias
norepinephrine	Levophed	2–30 mcg/min IV	For acute hypotension and severe shock

[a] Use caution with dosage (note concentrations).

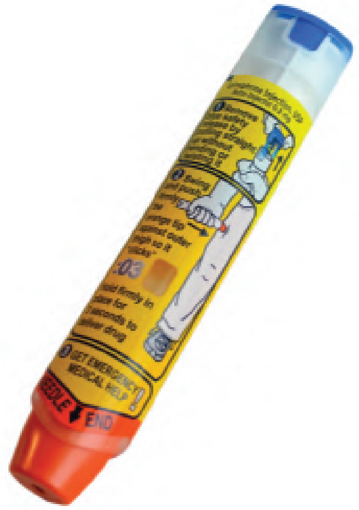


Figure 13-3 Epinephrine injector (EpiPen).

Infomages - Sam Lee / Shutterstock.com

Patient Education

Anaphylactic shock is a severe allergic reaction that occurs suddenly and is commonly caused by food, medication, or allergies (such as latex) in addition to severe reactions to insect bites or stings. Patients using epinephrine auto-injectors should be instructed regarding:

- Keeping this product near you at all times
- Learning in advance how to properly inject this medication in the thigh area only (epinephrine-training injectors are available)
- Teaching a family member or caregiver what to do if you cannot inject the medication yourself
- Seeking immediate medical attention after injection because the effects of this medication are rapid but not long-lasting
- Recognizing situations where a second dose (second pen) is needed such as a patient not responding, or not receiving the full initial dose because of user error (rushed or panicked situation)

Adrenergic Blockers

Just as certain medications can stimulate a receptor, there are specific medications that can block that receptor from having its normal response. Adrenergic blockers are also known as sympatholytic drugs because they work against the sympathetic response.

The most commonly used drugs in this category are the alpha- and beta-adrenergic blockers, or **alpha-blockers** and **beta-blockers**. Alpha-adrenergic blockers are discussed in more depth in the cardiovascular and urinary chapters.

Uses of the beta-blockers include treatment of the following:

Hypertension
Cardiac arrhythmias
Angina pectoris
Migraine headache
Tremor
Heart Failure
Emergency Scenarios

Side effects of beta-blockers may include:

Hypotension
❗ Bradycardia
❗ Fatigue or lethargy
❗ Bronchospasm
❗ Nausea and vomiting
❗ Hypoglycemia
❗ Confusion

Cautions/contraindications apply to the use of beta-blockers with:

Abrupt discontinuation (decrease over several weeks)
Congestive heart failure or atrioventricular block
Hypotension
Asthma, chronic obstructive pulmonary disease (COPD)
Diabetes (can mask signs of hypoglycemia)

Interactions of beta-blockers may occur with:

Digoxin (frequently used together; monitor for bradycardia)
Insulin or oral antidiabetic agents
Theophylline
MAOIs and tricyclic antidepressants
Epinephrine (causes hypertensive response)

Table 13-3 gives examples of some common beta-blockers and their indications.

Learning Hint

Think back to the snarling dog. The alpha-adrenergic response was to vasoconstrict to raise blood pressure, but if you block this response, you will vasodilate and lower blood pressure. The beta$_1$ adrenergic response was to increase your heart rate and force, but a beta-blocker would decrease your heart rate and force and thus lower the heart rate and lower blood pressure. That is why beta-blockers are used to treat high blood pressure and cardiac arrythmias that are going too fast (tachyarrhythmias).

Table 13-3 Representative Alpha- and Beta-Adrenergic Blockers

Generic Name	Trade Name	Dosage	Comments
Beta-Adrenergic Blockers			
propranolol[a]	Inderal[b]	PO 10–320 mg daily; IR formulations can be taken in divided doses up to four times daily ER formulations are usually taken one to two times daily	Begin with smaller dose and increase gradually to optimum dose for blood pressure control Also used for angina (low dose), arrhythmias, and migraine prevention
	Inderal LA	PO 80–160 mg daily	Extended-release capsules
metoprolol tartrate[a]	Lopressor[b]	PO 25–100 mg divided into two to three doses daily	Treat hypertension Can titrate up as tolerated up to 450 mg max daily dose
metoprolol succinate[a]	Toprol XL Kapspargo Sprinkles	PO 25–200 mg one to two times daily PO 25–100 mg daily	Toprol XL tablets are unique in that they can be cut/split Kapspargo Sprinkle capsules can be sprinkled on food such as applesauce
Alpha-Adrenergic Blockers			
doxazosin[c]	Cardura Cardura XL	PO 1–2 mg daily in A.M. or P.M. Can titrate up to 16 mg max daily dose	Used for hypertension and BPH
tamsulosin[c]	Flomax	PO 0.4 mg daily Max dose of 0.8 mg daily	Used for BPH Taken after same meal each day

[a] A beta-adrenergic blocker or beta-blocker. Others are available and vary with condition.
[b] This brand name is no longer marketed, but the name is still commonly used.
[c] An alpha-adrenergic blocker. Others are available and vary with condition.

Patient Education

Patients taking beta-blockers, frequently given for cardiovascular disease, should be instructed regarding:

Rising slowly from a reclining position to avoid postural hypotension

Reporting possible slow heartbeat and dizziness, difficulty breathing, or excessive weakness to the physician

If you have diabetes, checking with your health care professional before changing diet or the dose of your diabetic medication

Avoiding alcohol, antihistamines, muscle relaxants, tranquilizers, and sedatives because they potentiate CNS depression and sedation

Reporting sexual dysfunction or depression to the physician for possible dosage regulation or change to different medication

Not discontinuing the medication abruptly, except on advice of the physician

Consulting a physician or pharmacist before using over-the-counter (OTC) cold preparations

Clinical Application

Patient Compliance with Adrenergic Blockers

Patient compliance with adrenergic blockers (also called beta-blockers) when taken orally is poor. Beta-blockers are often discontinued or not taken regularly by patients because of various side effects; the most common of these is fatigue. Many times this can be resolved by using an extended release formulation, dividing doses throughout the day, or taking a single dose at night.

Cholinergics

The neurochemical transmitter used throughout the parasympathetic nervous system is acetylcholine (ACh); therefore, drugs that stimulate or mimic the parasympathetic nervous system are called parasympathomimetic or **cholinergic drugs**.

The word *para* means "working beside," and the parasympathetic system works beside the sympathetic system to bring you back to homeostasis after a crisis, such as the previously mentioned snarling dog, is over. Therefore, the responses include lowering heart rate and pressure, bronchoconstriction, and pupil constriction. Also keep in mind that this system is your resting and digesting system, so while you are going about your daily routine, the parasympathetic system is producing secretions and taking care of digestion and urinary functions.

Actions of the cholinergics include:

Increased gastrointestinal (GI) peristalsis
Increased contraction of the urinary bladder
Increased secretions (sweat, saliva, and gastric juices)
Increased skeletal muscle strength
Lowered intraocular pressure
Constriction of the pupils
Slowing of the heart

Uses of the cholinergics include treatment of:

Nonobstructive urinary retention (bethanechol)
Neuromuscular blockade reversal (neostigmine)
Myasthenia gravis (pyridostigmine)
Xerostomia (dry mouth) (pilocarpine—Salagen)
Open-angle glaucoma (pilocarpine)

Side effects of the cholinergics may include:

- ❗ Nausea, vomiting, and diarrhea
- ❗ Muscle cramps and weakness
- ❗ Slowing of the heart and hypotension

- ❗ Sweating, excessive salivation, lacrimation (discharge of tears), and flushing
- ❗ Respiratory depression and bronchospasm

Cautions/contraindications for the cholinergics apply to those with:

- Benign prostatic hyperplasia (BPH)
- GI disorders (e.g., ulcer and obstruction)
- Asthma
- Cardiac disorders
- Hyperthyroidism

Interactions of cholinergics may occur with:

- Procainamide and quinidine (have anticholinergic properties)
- Local anesthetics (inhibit neuronal transmission in skeletal muscles)

Table 13-4 provides a summary of the cholinergics.

Clinical Application

Overstimulation of the parasympathetic system can be dangerous. Certain nerve gases and insecticides can overstimulate the system and cause your heart to slow to a dangerous rate and cause severe bronchoconstriction, making it difficult to breathe. Overstimulation of the parasympathetic nervous system is known as a cholinergic crisis. Acute toxicity or cholinergic crisis is treated with atropine sulfate IV. Atropine is a cholinergic blocker and therefore would block the effects of a cholinergic crisis.

Table 13-4 Representative Cholinergic Medications

Generic Name	Trade Name	Dosage	Comments
bethanechol	Urecholine	10–50 mg PO three to four times per day	For postpartum or postoperative urinary retention, *not* with benign prostatic hyperplasia (BPH)
cevimeline	Exovac	PO 30 mg capsule q8h	For xerostomia
neostigmine	Prostigmin	0.5–2.5 mg IM, SQ or IV q1–3h	Primarily for neuromuscular blockade reversal
pilocarpine	Isopto Carpine	Ophthalmic drops; dose varies	To lower intraocular pressure in glaucoma
pyridostigmine	Salagen	5 mg PO three to four times per day	For the treatment of xerostomia (dry mouth)
	Mestinon Timespan	180–540 mg PO one to two times per day	Primarily for the treatment of myasthenia gravis

Patient Education

Patients taking cholinergic drugs, or exposed to insecticides containing cholinergic agents (e.g., malathion), should be instructed regarding:

- Reporting immediately to a physician or an emergency department any symptoms of prolonged GI distress (e.g., nausea, vomiting, and diarrhea), excessive perspiration, slow heartbeat, or depressed respiration
- Avoiding any combination of cholinergic medications with heart medications or cholinergic blockers

Cholinergic Blockers

Cholinergic blockers, or **anticholinergics**, are drugs that block the action of the parasympathetic nervous system. Therefore, they are also called parasympatholytics. Remember the parasympathetic nervous system is normally producing secretions and performing digestion, so blocking these functions would cause decreased secretions and decreased GI motility. A common use of anticholinergics is scopolamine transdermal patches to treat or prevent seasickness by decreasing gastric secretions and motility. Anticholinergic eye drops can be used to dilate the eyes by causing relaxation of the muscles of the iris (colored part of the eye), which is normally stimulated to constrict by acetylcholine, a parasympathetic response.

Anticholinergics most commonly used as preoperative medications include atropine and glycopyrrolate (Robinul). They reduce the secretions of the mouth, pharynx, bronchi, and GI tract and reduce gastric activity, which is beneficial during surgery. Anticholinergics, as preoperative medications, are also used to prevent cholinergic effects during surgery, such as hypotension or bradycardia and some cardiac arrhythmias associated with general anesthetics or vagal stimulation. The vagus nerve is the major nerve of the parasympathetic nervous system and can be stimulated during intubation procedures and surgery. However, only *atropine* acts as a bronchodilator and reduces the incidence of laryngospasm that can occur during general anesthesia.

Actions of anticholinergics include:

Drying (all secretions decreased)
Decreased GI and genitourinary (GU) motility
Dilation of the pupils

Uses of the anticholinergics include:

Antispasmodic and antisecretory for GI or GU hypermotility
Preoperative and preanesthetic uses
Antidote for insecticide poisoning, cholinergic crisis, or mushroom poisoning
Emergency treatment of bradycardia and atrioventricular heart block with hypotension

Clinical Application

In practice, there are situations when it is necessary to dilate the pupils of the eyes, that is, making the pupils bigger and wider. The most common eye drop used is atropine, which is an anticholinergic ophthalmic eye drop. When a patient goes to the eye doctor, it is often easier to diagnose or treat diseases of the eye if the pupils are dilated because they are more open for the doctor to view the back of the eyes. Additionally, dilating the pupils makes it easier to make some measurements for eyeglasses. It is important to educate patients that after leaving their appointment, their eyes will be more sensitive to light, as atropine drops keep the eyes dilated for between 4 and 24 hours. This means patients should wear sunglasses in well-lit areas for the rest of the day. Atropine can also be used as a maintenance treatment for various eye conditions such as conjunctivitis. These patients should be instructed to wear eye protection and be cautious in well-lit areas.

Dilation of the pupils (mydriatic)

Prevention and treatment of bronchospasm (bronchodilator, e.g., Atrovent HFA [Hydrofluroalkane] inhaler)

Side effects of anticholinergics may include:

Fever or flushing

❗ Blurred vision and headache

❗ Dry mouth, constipation, and urinary retention

❗ Falls, delirium, and cognitive impairment, especially in older adults

❗ Palpitations and tachycardia (abnormally fast heartbeat)

Interactions with potentiation of sedation and drying occur with:

Antihistamines (e.g., diphenhydramine)

Cautions/contraindications apply to the use of atropine for those with:

Asthma and other COPD—atropine-type *inhalations of aerosols are recommended* rather than oral or parenteral administration, which can reduce and dry bronchial secretions and obstruct airflow

Angle-closure glaucoma

GI or GU obstruction

Cardiac arrhythmias

Hypertension

Hypothyroidism and hepatic or renal disease

Table 13-5 provides a summary of the anticholinergics.

Table 13-5 Representative Cholinergic Blockers

Generic Name	Trade Name	Dosage[a]	Comments
atropine		0.4–0.6 mg IM, IV, SQ 0.5–1 mg IV	Preoperative For bradycardia
		1% ophthalmic: 1–2 drops 1 h before needed	For pupil dilation
scopolamine	Transderm-Scop	72-h patch	Prevents motion sickness; reduces salivary flow
	Donnatal[b]	One to two tabs three to four times per day	For irritable bowel syndrome
homatropine	Isopto Homatropine	Dosage varies for ophthalmic drops[a]	Mydriatic
dicylomine	Bentyl	PO 10–20 mg q6h tablet or capsule	For irritable bowel syndrome
fesoterodine	Toviaz	PO 4–8 mg daily (ER tablet)	For overactive bladder
oxybutynin	Ditropan XL	PO 5–10–15 mg daily in ER tablets	For overactive bladder

[a] Other anticholinergics used in ophthalmic conditions are discussed in Chapter 18.

[b] With atropine, hyoscyamine, and phenobarbital.

Learning Hint

A memory tool to help with the major effects of cholinergic blockers is to think "3-D effects." These include (1) drying of secretions, (2) decreased motility (GI and urinary system), and (3) dilated pupils.

Patient Education

Patients receiving cholinergic blockers should be instructed regarding:

Dried secretions (e.g., dry mouth)

Possible blurring of vision

Reporting fast heartbeat or palpitations, feeling faint or falls, or trouble passing urine

Avoiding oral anticholinergics with chronic obstructive lung disease and asthma and using inhalants only as prescribed, never OTC

Case Study A

ANS Drugs

A patient who has a severe allergy to shrimp inadvertently ingests shrimp that was diced into pieces so small they did not notice them in their salad. They begin to experience signs of a severe reaction to the shrimp such as throat tightening and lip and eyelid swelling.

1. Which medication would be used as the first-line treatment for the patient's symptoms?
- a. Levophed
- b. Neo-Synephrine
- c. Adrenalin
- d. Isuprel

2. When a patient is given an adrenergic medication, which action does the medication have on the ANS?
- a. It mimics a sympathetic response.
- b. It blocks a sympathetic response.
- c. It mimics a parasympathetic response.
- d. It blocks a parasympathetic response.

3. The EpiPen delivers an adrenergic medication, which has a primary effect of
- a. constriction of the pupils
- b. bronchodilation
- c. peripheral vasodilation
- d. cardiac relaxation

4. A side effect the patient may experience after the EpiPen injection is
- a. bradycardia
- b. palpitations
- c. migraine headache
- d. hypotension

5. Which part of the ANS helps the body to be ready for emergencies?
- a. parasympathetic
- b. parasympahtolytic
- c. cholinergic
- d. sympathetic

Case Study B

Cholinergic Blockers

A 30-year-old patient is enjoying a Caribbean cruise on their honeymoon. However, on the second day of the cruise, they start to feel queasy and seasick. Their nausea is so bad they tell their spouse they want to get off the ship at the next port. Their spouse suggests that they visit the ship's clinic first for treatment.

1. Which type of drug will most likely be prescribed by the ship's physician?
   a. beta-blocker
   b. antihistamine
   c. cholinergic
   d. anticholinergic
2. Scopolamine is prescribed. This medication will most likely be delivered by which route?
   a. IM
   b. IV
   c. patch
   d. PO
3. When educating the patient about scopolamine, the ship's physician will tell them that they may experience:
   a. nausea
   b. dry mouth
   c. sweating
   d. slower heart rate
4. Which of the following medications in the same class as scopolamine reduces the incidence of laryngospasm that can occur with general anesthesia?
   a. glycopyrrolate
   b. norepinephrine
   c. ephedrine
   d. atropine
5. Which of the following medications is often given preoperatively to reduce the secretions of the mouth and pharynx?
   a. Robinul
   b. Isopto Homatropine
   c. Levophed
   d. Urecholine

Chapter Review Quiz

Match the type of drug with the action. Each type of drug may be used more than once.

Action

1. _______ Increases muscle strength
2. _______ Drying secretions
3. _______ Increases blood pressure
4. _______ Increases peristalsis
5. _______ Lowers intraocular pressure
6. _______ Antispasmodic
7. _______ Bronchodilator
8. _______ Lowers blood pressure
9. _______ Constricts pupils
10. _______ Antiarrhythmic

ANS Drugs

a. Adrenergic
b. Adrenergic blocker
c. Cholinergic
d. Anticholinergic

Match the type of drug with possible side effects. Each type of drug may be used more than once.

Side Effects

11. _______ Bronchospasm
12. _______ Hyperglycemia
13. _______ Diarrhea
14. _______ Flushing
15. _______ Lethargy
16. _______ Hypoglycemia
17. _______ Constipation
18. _______ Nervousness
19. _______ Cognitive impairment

ANS Drugs

a. Adrenergic
b. Adrenergic blocker
c. Cholinergic
d. Anticholinergic

20. A cholinergic drug should be used with extreme caution in a patient with

a. benign prostatic hyperplasia (BPH)
b. hepatic disease
c. hypothyroidism
d. renal disease

Chapter 14

Cardiovascular System Medications

Key Terms and Concepts

Antiarrhythmic agents
Anticoagulants
Antihypertensives
Antilipemic agents
Antithrombotic agents
Arrhythmia
Bradycardia
Coronary heart disease (CHD)
Coronary vasodilators
Heart failure
Hematopoiesis
Hypertension
Hypotension
Ischemia
Platelet inhibitors
Tachycardia
Thrombolytic agents

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify the different types of antiarrhythmics, general indications, side effects, and toxicities.
2. Classify the most commonly used antihypertensives and their side effects.
3. Describe the different types of coronary vasodilators and their cautions and side effects.
4. Cite examples of the six antilipemic categories and describe their actions.
5. Describe antithrombotic agents in terms of administration, action, typical drugs, and antidotes.
6. Explain appropriate and important patient education for all cardiovascular system medications.

The cardiovascular system consists of the heart, which is a muscular organ, and a system of vessels called arteries, veins, and capillaries. The blood contained in the circulatory system is pumped by the heart around a loop or circuit of vessels. Blood is needed to supply oxygen and nutrients to all parts of the body. Since the cardiovascular system serves such an important role, it is crucial that you understand the various medication classes that treat its ailments and conditions.

Cardiovascular drugs include medications that affect the heart and blood vessels as well as anticoagulant and antiplatelet agents that prevent clotting. The drugs described in this chapter are divided into the following categories: cardiac glycosides, antiarrhythmic agents, antihypertensives, vasodilators, antilipemic agents, anticoagulants, platelet inhibitors, thrombolytics, and hematopoietic agents. Some of the drugs described in this chapter fall into more than one category because of their multiple actions and uses (e.g., propranolol, which is used to treat cardiac arrhythmias, hypertension, and angina).

Cardiac Glycosides (Digoxin)

Cardiac glycosides occur widely in nature and can be prepared synthetically. These glycosides act directly on the myocardium to increase the force of myocardial contractions. Digoxin is the only clinical drug currently used in the cardiac glycoside family. It is used primarily in the treatment of heart failure in patients with symptoms that persist after optimization of treatment with an ACE inhibitor, a beta-adrenergic blocker, and/or a diuretic. It is sometimes also used alone or in conjunction with other medications (such as calcium channel blockers) to *slow* the ventricular response in patients with atrial fibrillation or flutter.

In patients with heart failure, the heart fails to adequately pump nutrients and oxygen to body tissues. Because the heart is failing, the body attempts to compensate by retaining salt and fluid, and this may result in both pulmonary and peripheral edema. The heart increases in size to compensate for the increased workload. Symptoms of heart failure include fatigue, weakness, dyspnea, cyanosis, increased heart rate, cough, and pitting edema.

Clinical Application

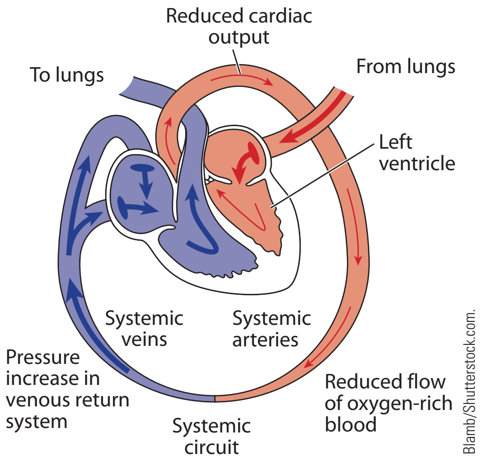
Patient Information Interviews

One of the most overlooked practices conducted by health care professionals is interviewing new or unfamiliar patients about their medications and disease states. This is important because medications can be used for multiple indications. Some disease states do not have medications that are unique to their treatment. **Heart failure** (HF) is a common condition that can result from other disease states and also cause complications. Although the diagnosis of HF is fairly straightforward, treatment can be complicated and vary drastically from patient to patient. HF patients are almost always prescribed three main classes of medications: (1) Certain beta-blockers (bisoprolol, carvedilol, and metoprolol) are approved to treat HF and act to slow the heart rate; (2) angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs); and (3) diuretics.

Additional medications can be added, including digoxin, nitrates, or hydralazine (vasodilators) and aldosterone antagonists. All these medication options are indicated in other disease states, so it may not be easy to recognize that a person has heart failure with just a quick review of their medications; therefore, it is important to be thorough during patient interviews to avoid prescribing a drug that is contraindicated in patients with HF.

In patients with heart failure, digoxin *increases the force of the cardiac contractions* without increasing oxygen consumption, thereby increasing cardiac output. It also lowers norepinephrine levels, which are elevated in heart failure and are toxic to the failing heart. As a result of increased efficiency, the heart beats more slowly, the heart size shrinks, and the concurrent diuretic therapy decreases edema. Refer to Figure 14-1 to learn how heart failure manifests in the body.

There is a very narrow margin between effective therapy with digoxin and dangerous toxicity, meaning digoxin is considered to be a narrow therapeutic index (NTI) drug. Careful monitoring of cardiac rate and rhythm with EKG (electrocardiogram), cardiac function, side effects, and serum digoxin levels is required to determine the therapeutic maintenance dose. Checking the apical pulse before administering digoxin is an important part of this monitoring process. If the apical pulse rate is less than 60 beats per minute, digoxin may need to be withheld until the physician is consulted.


Reduced cardiac output
To lungs
From lungs
Left ventricle
Systemic veins
Systemic arteries
Pressure increase in venous return system
Systemic circuit
Reduced flow of oxygen-rich blood

Blamb/Shutterstock.com.

Figure 14-1 Heart failure results in a decreased cardiac output, which leads to a lack of oxygenated blood from the lungs to be pumped throughout the body.

Toxic side effects of digoxin, which should be reported to the physician immediately, can include:

- ❗ Anorexia, nausea, and vomiting (early signs of toxicity)
- ❗ Fatigue, lethargy, and muscle weakness
- ❗ Vertigo, restlessness, irritability, tremors, and seizures
- ❗ Visual disturbances, including blurring, diplopia (double vision), and visual halos (halos are unique to digoxin toxicity)
- ❗ Bradycardia (rate less than 60 beats per minute)
- ❗ Insomnia, confusion, and mental disorders, especially with older adults

Treatment of digoxin toxicity includes:

Discontinuing the drug immediately (usually sufficient)

Monitoring electrolytes for hyperkalemia, hypokalemia, hypomagnesemia, and hypercalcemia

Drugs such as atropine for symptomatic bradycardia

Digoxin-specific Fab fragments (DigiFab) as an antidote in life-threatening toxicity

Cautions or contraindications for the use of digoxin apply to:

Severe pulmonary disease

Hypothyroidism

Acute myocardial infarction, acute myocarditis, and severe heart failure

Impaired renal function (hypokalemia and hypomagnesemia)

Arrhythmias not caused by heart failure

Pregnancy and lactation

High doses in older adults

Interactions of digoxin may occur with:

Antacids, cholestyramine, neomycin, and rifampin (reduce the absorption of digoxin; administer at least 2-4 hours apart)

Diuretics, calcium, and corticosteroids (can increase the chance of arrhythmias)

Macrolides and antiarrhythmics (*especially* quinidine and verapamil) may potentiate digoxin toxicity

Adrenergics (epinephrine, ephedrine, and isoproterenol; increase the risk of arrhythmias)

Patient Education

Patients taking digoxin should be instructed regarding:

- Recognition and immediate reporting of side effects
- Holding medication, if any side effects occur, until the physician can be consulted
- Avoiding taking any other medication at the same time without physician approval
- Avoiding all over-the-counter (OTC) medication, especially antacids and cold remedies
- Avoiding abrupt withdrawal after prolonged use; must be reduced gradually under physician supervision
- Checking heart rate (pulse) on a regular basis

Antiarrhythmic Agents

The term **arrhythmia** refers to any change from the normal sequence of electrical impulses of the heart. The electrical impulses may happen too quickly, too slowly, or erratically, causing the heart to beat too quickly (**tachycardia**), too slowly (**bradycardia**), or erratically (fibrillation). **Antiarrhythmic agents** include a variety of drugs that act in different ways to suppress various types of cardiac arrhythmias. The choice of a particular antiarrhythmic agent is based on a careful assessment of many factors, including the type of arrhythmia; frequency; cardiac, renal, or other pathological condition; and current signs and symptoms.

The role of the health care professional is critical in this area in accurate and timely reporting of vital signs, pertinent observations regarding the effectiveness of medications and adverse side effects, and modification of precipitating causes. Adequate knowledge of drug action and effects, along with good judgment, is essential.

Side effects of the individual medications are discussed separately. However, keep in mind that most of the drugs given to counteract arrhythmias have the potential for lowering blood pressure and slowing heartbeat. Therefore, it is especially important to be alert for the signs of **hypotension** and bradycardia, which could lead to cardiac arrest. Although antiarrhythmics commonly slow the heart rate, there are exceptions (e.g., procainamide and quinidine, which may cause *tachycardia*). When other cardiac drugs are administered concomitantly, cardiac effects may be additive or antagonistic. Antiarrhythmic agents can worsen existing arrhythmias or cause new arrhythmias, and therefore *careful monitoring is essential.*

Arrhythmia detection or monitoring can include EKG rhythm strips and 24-hour Holter monitoring as indicated. Electrolyte surveillance, especially for disorders of potassium and magnesium, is very important for patients on antiarrhythmic agents. Nondrug therapy can include the insertion of a pacemaker or an implantable cardioverter-defibrillator (ICD). The ICD has been widely accepted as the most effective treatment for patients with life-threatening ventricular tachycardia or fibrillation and for patients who have survived a cardiac arrest, and the ICD may also be effective in preventing sudden death in certain patients with heart failure. Antiarrhythmic drug classes are summarized in Figure 14-1.

Adenosine

Adenosine (Adenocard) is an injectable antiarrhythmic agent with multiple electrophysiological activities that complicate its placement into a single category. It restores normal sinus rhythm in paroxysmal supraventricular tachycardia (PSVT) by slowing conduction time through the atrioventricular (AV) node. Adenosine also has vasodilatory, antiadrenergic, and negative chronotropic (decrease in rate) properties, which act to decrease cardiac oxygen demand.

Adenosine is equal in effectiveness to diltiazem or verapamil in converting PSVT but is less likely to cause hypotension. Common side effects include facial flushing, lightheadedness, headache, dyspnea, and chest pressure. Adenosine is contraindicated in patients with a second- or third-degree heart block or symptomatic bradycardia (unless a functioning artificial pacemaker is present).

Amiodarone

Amiodarone (Cordarone) is an oral and injectable antiarrhythmic agent approved for the treatment of refractory life-threatening ventricular arrhythmias. Despite its problematic organ toxicity profile and black box warning, amiodarone is widely used for preventing the recurrence of atrial fibrillation. It is considered a broad-spectrum antiarrhythmic with multiple and complex electrophysiological effects. Amiodarone also relaxes both smooth and cardiac muscle, causing decreases in coronary and peripheral vascular resistance and systolic blood pressure.

Side effects of amiodarone, some of which are severe and potentially fatal, but may be less of a problem with lower doses (i.e., 200–400 mg per day), include:

Pulmonary fibrosis

❗ Cardiac arrhythmias, induction or worsening of heart failure, and hypotension

Hepatitis (rare)

Neurotoxicity (tremor, peripheral neuropathy, paresthesias [numbness, tingling, especially in extremities])

Visual disturbances; optic neuropathy and/or neuritis (may progress to permanent blindness)

Dermatological reactions, especially photosensitivity (avoid exposure, wear protective clothing)

Cautions or contraindications for amiodarone apply to:

Patients with a second- or third-degree heart block, marked sinus bradycardia because of severe sinus node dysfunction, and when bradycardia has caused syncope (unless a functioning artificial pacemaker is present); cardiogenic shock

Patients with thyroid disease (because of the large amount of iodine contained in amiodarone)

Iodine hypersensitivity

Older adults (more susceptible to thyrotoxic and neurotoxic adverse effects)

Interactions with amiodarone are numerous and significant, including:

Certain fluoroquinolones, macrolide antibiotics, systemic azole antifungals (QT prolongation)

❗ Warfarin (can result in serious or fatal bleeding if warfarin dose is not reduced; effect may persist for months after discontinuation)

Certain antiarrhythmics, digoxin, and phenytoin (amiodarone increases serum concentrations of these drugs)

Protease inhibitors and grapefruit juice (increase amiodarone concentrations); beta-blockers, calcium channel blockers, and lidocaine (additive adverse cardiac effects)

Cholestyramine, phenytoin, and rifampin (serum concentrations of amiodarone are decreased, reducing its pharmacologic effect)

Beta-Adrenergic Blockers

Beta-adrenergic blockers, for example, propranolol (Inderal), are antiarrhythmics, which combat arrhythmias by inhibiting adrenergic (sympathetic) nerve receptors. The action is complex, and the results can include a membrane-stabilizing effect on the heart. Propranolol (Inderal), a nonselective beta-blocker, is effective in the management of some cardiac arrhythmias and less effective with others. It is also used in the treatment of hypertension and some forms of chronic angina. Because it also blocks the beta$_2$ receptors in the lungs, it can lead to bronchospasm. *Low doses* of metoprolol (Lopressor), a selective beta$_1$ antagonist, may be used *with caution* in patients with lung conditions that cause bronchospasm.

Side effects of beta-blockers, especially in patients over 60 years old (and more commonly with the IV administration of the drug), can include:

❗ Hypotension, with vertigo and syncope

❗ Bradycardia, with (rarely) heart block and cardiac arrest

❗ CNS symptoms (usually with long-term treatment with high doses), including dizziness, irritability, confusion, nightmares, insomnia, visual disturbances, weakness, sleepiness, lassitude, or fatigue

GI symptoms, including nausea, vomiting, and diarrhea or constipation

Rash or hematological effects (rare or transient)

❗ Bronchospasm, especially with a history of asthma (more common at higher doses and with non-selective beta-blockers)

❗ Hypoglycemia

Impotence (reported rarely)

Cautions or contraindications for the use of beta-blockers apply to:

- Withdrawal after prolonged use (should always be gradual)
- Withdrawal before surgery (weigh risk versus benefits)
- Diabetes (may cause hypoglycemia and mask the tachycardic response to hypoglycemia)
- Renal and hepatic impairment
- Asthma and allergic rhinitis (may cause bronchospasm)
- Bradycardia, heart block, and congestive heart failure (CHF)
- Pediatric use
- Pregnancy and lactation
- Chronic obstructive pulmonary disease (COPD)

Learning Hint

Beta$_1$ receptors are found primarily in the heart and when stimulated cause an increase in the rate and force of contraction. Beta$_2$ receptors are found primarily in the lungs (when stimulated, they cause relaxation or bronchodilation of airways) and blood vessels (when stimulated, they cause vasodilation). A useful mnemonic is to think how many hearts you have (one) and how many lungs (two): The class of selective *beta$_1$-blockers* would therefore decrease the rate and force of contraction of the heart and, if nonselective, may also cause bronchospasm and mild vasoconstriction of blood vessels.

Interactions include *antagonism* of beta-blockers by:

- Adrenergics (e.g., epinephrine and isoproterenol)
- NSAIDs and salicylates
- Tricyclic antidepressants

Potentiation of the *hypotensive effect* of propranolol occurs with:

- Diuretics and other antihypertensives, for example, calcium channel blockers
- MAOIs; phenothiazine and other tranquilizers
- Cimetidine (Tagamet), which slows metabolism of the drug
- Certain antiarrhythmic drugs (e.g., adenosine, digoxin, and quinidine), which may potentiate toxic effects
- Alcohol, muscle relaxants, and sedatives, which may precipitate hypotension, dizziness, confusion, or sedation

Calcium Channel Blockers

Of the calcium channel blockers available, only verapamil (Calan) and diltiazem (Cardizem) possess significant antiarrhythmic activity. These agents are indicated for the treatment of atrial fibrillation/flutter and PSVT. Verapamil and diltiazem counteract arrhythmias by slowing AV nodal conduction. Calcium channel blockers are also used in the treatment of angina and hypertension.

Side effects of calcium channel blockers can include:

- ❗ Hypotension, with vertigo and headache
- ❗ Bradycardia, with heart block
- ❗ Edema
- ❗ Constipation, nausea, and abdominal discomfort

Note

Do not drink grapefruit juice with certain calcium channel blockers because adverse effects may be potentiated.

Cautions or contraindications for calcium channel blockers apply to:

Heart block, heart failure, or angina
Hepatic and renal impairment
Pregnancy and lactation
Children
Hypotension and heart block
Certain arrhythmias and severe heart failure

Interactions of calcium channel blockers with other cardiac drugs, for example, digoxin, can potentiate both good and adverse effects.

Antagonistic effects with calcium channel blockers include:

Barbiturates, cimetidine, phenytoin, ranitidine, and rifampin
Hypotensive effect potentiated with diuretics, ACE inhibitors, beta-blockers, and quinidine

Lidocaine

Local anesthetics (e.g., lidocaine) are administered for their antiarrhythmic effects and membrane-stabilizing action. Lidocaine has historically been used as a first-line antiarrhythmic agent for acute, life-threatening ventricular arrhythmias. However, it is now considered a second choice behind other alternative agents (e.g., IV amiodarone) for the treatment of ventricular arrhythmias. EKG monitoring and availability of resuscitative equipment are necessary during the IV administration of lidocaine.

Side effects of lidocaine are usually of short duration, are dose related, and can include:

- ❗ CNS symptoms, including tremors, seizures, dizziness, confusion, and blurred vision
- ❗ Hypotension, bradycardia, and heart block
- ❗ Dyspnea, respiratory depression, and arrest

Cautions or contraindications with lidocaine apply to:

Patients hypersensitive to local anesthetics of this type (amide type)
Heart block and respiratory depression
Pregnancy and lactation
Children

Procainamide

Procainamide, quinidine, and disopyramide (Norpace) are antiarrhythmic agents. They act by decreasing myocardial excitability and inhibiting conduction, and they may depress myocardial contractility. These agents possess anticholinergic properties.

IV procainamide is a potential treatment alternative (to amiodarone) for the treatment of ventricular tachycardia during cardiopulmonary resuscitation. These agents are used orally primarily as prophylactic therapy to maintain normal rhythm after conversion by other methods.

Side effects of this class of antiarrhythmics are numerous and may necessitate cessation of treatment. They may include:

❗ Diarrhea, anorexia, nausea and vomiting, and abdominal pain (which are common)
❗ Tachycardia, QT prolongation, hypotension, and syncope
❗ Anticholinergic effects, including dry mouth, blurred vision, confusion, constipation, and urinary retention
❗ Vascular collapse and respiratory arrest with IV administration
Vision abnormalities or hearing disturbances (with quinidine)
Blood dyscrasias, including anemia, clotting deficiencies, and leukopenia (relatively rare)
Hepatic disorders; fever
❗ Dermatological effects, including rash, pruritis, and urticaria

Cautions or contraindications with these agents apply to:

Atrioventricular block and conduction defects
Electrolyte imbalance
Digoxin toxicity
Heart failure and hypotension
Myasthenia gravis
Older adults—more susceptible to hypotensive and anticholinergic effects
Children
Pregnancy and lactation
Hepatic or renal disorders
Hypersensitivity to "ester-type" local anesthetics with procainamide
Systemic lupus erythematosus (SLE) with procainamide

Interactions with increased possibility of toxicity may occur with:

Muscle relaxants and neuromuscular blockers
Anticholinergics, tricyclic antidepressants, and phenothiazines
Other cardiac drugs, especially digoxin and antihypertensives

Interactions with increased possibility of *quinidine* toxicity may occur with:

Antiretroviral protease inhibitors
Antacids or sodium bicarbonate
Anticonvulsants (e.g., phenytoin and phenobarbital; cause decreased serum levels)
Anticoagulants (action can be potentiated by quinidine)

Propafenone

Propafenone (Rythmol) is an oral antiarrhythmic agent used to treat symptomatic supraventricular arrhythmias or severe, life-threatening ventricular arrhythmias. It is also useful in converting atrial fibrillation to sinus rhythm and maintaining it. Propafenone has local anesthetic effects, direct stabilizing action on myocardial membranes, and beta-adrenergic blocking properties.

Side effects of propafenone may include:

- Dizziness and blurred vision
- Nausea, vomiting, unusual taste, and constipation
- Angina, heart failure, palpitations, arrhythmia, and dyspnea
- Fatigue, weakness, and headache
- Rash

Cautions or contraindications include:

- Asthma or acute bronchospasm
- Second- or third-degree heart block (in the absence of a pacemaker), cardiogenic shock, heart failure, and bradycardia
- Marked hypotension and electrolyte imbalance

Interactions of propafenone may occur with:

- Quinidine, ritonavir, and certain selective serotonin reuptake inhibitors (SSRIs) (may cause serum levels of propafenone to be elevated)
- Beta-blockers, digoxin, and theophylline (may result in increased serum levels of the same)

Patient Education

Patients taking antiarrhythmics should be instructed regarding:

- Immediate reporting of adverse side effects, especially palpitations, irregular or slow heartbeat, faintness, dizziness, weakness, respiratory distress, and visual disturbances
- Holding the medication, if there are side effects, until the physician is contacted
- Rising slowly from a reclining position
- Modification of lifestyle to reduce stress
- Mild exercise on a regular basis as approved by the physician
- Not discontinuing the medicine, even if the patient feels well
- Taking the proper dosage of the medication on time, as prescribed, without skipping any dose
- If the medication is forgotten, not doubling the dose
- Taking the medication with a full glass of water on an empty stomach, 1 h before or 2 h after meals, so that it will be absorbed more efficiently (unless stomach upset occurs or the physician prescribes otherwise)
- Avoiding taking any other medication, including OTC medicines, unless approved by the physician
- Discarding expired medicines and renewing the prescription
- Avoiding comparisons with other patients on similar drugs
- Contacting the physician immediately with any concerns regarding medicines

Table 14-1 provides a summary of cardiac glycosides and the antiarrhythmics.

Table 14-1 Cardiac Glycosides and Antiarrhythmics

Generic Name	Trade Name	Dosage	Comments[b]
Cardiac Glycoside			
digoxin	Lanoxin	PO: tablets, elixir IM, IV, dosage varies	Monitor serum levels (0.5–0.8 mg/mL for heart failure; 0.8 –2 mg/mL for afib)
Antiarrhythmics (Grouped by Class)			
IA procainamide		IV	For VTach, afib, PAT, PSVT; has anticholinergic properties
IB lidocaine	Xylocaine	IV diluted	Local anesthetic—amide type for Vfib, VTach; check IV dilution directions
IC propafenone	Rythmol Rythmol SR	PO, 150–300 mg q8h PO, 225–425 mg q12h	For afib, PSVT, VTach For afib prevention
II metoprolol[a]	Lopressor	PO, 25–100 mg bid IV, 2.5–5 mg IV bolus, repeat q5 min for three doses total	Beta-blocker for heart rate control in afib
III amiodarone	Cordarone, Pacerone	IV, PO; dose varies	For ventricular arrhythmias; also a vasodilator; medication guide required
IV verapamil[a]	Calan	IV 2.5–10 mg; PO 240–480 mg daily in divided doses	Calcium channel blocker for afib and PSVT
V[c] adenosine	Adenocard	IV bolus 6 mg; then 12 mg PRN up to 30 mg	For PSVT; do not confuse with amiodarone

Note: Other antiarrhythmics are available. This is a representative sample by classification.

[a] afib = atrial fibrillation; PAT = paroxysmal atrial tachycardia; PSVT = paroxysmal supraventricular tachycardia; Vfib = ventricular fibrillation; VTach = ventricular tachycardia.

[b] Has other cardiac uses.

[c] Digoxin is often classified in class V when used as an antiarrhythmic agent.

Antihypertensives

Hypertension is a widespread epidemic that affects as many as 1.3 billion people worldwide and more than120 million adults in the United States. According to the AHA and CDC 2020 guidelines, hypertension is defined as regular resting systolic blood pressure (SBP) of 130 or greater or diastolic blood pressure (DBP) of 90 or greater. There is a strong, consistent relationship between blood pressure (BP) and the risk of cardiovascular disease (CVD). High blood pressure increases the risk of angina, myocardial infarction, heart failure, stroke, retinopathy, peripheral arterial disease, and kidney disease and thus requires aggressive treatment.

An additional 59 million adults in the United States are considered to have *prehypertension* (SBP range of 120–129 and DBP range of 80–89), a condition that may identify patients who are at a higher cardiovascular risk based on BP and a higher risk for developing sustained hypertension in later years. The purpose of this classification is to encourage patients to initiate or continue healthy lifestyle practices, rather than to begin antihypertensive drug therapy. Such practices include weight reduction (in patients who are overweight or obese), use of the *Dietary Approaches to Stop Hypertension* (DASH) eating plan, dietary sodium reduction, increased physical activity, modified alcohol use, and smoking cessation.

Antihypertensives do not cure hypertension; they only control it. After withdrawal of the drug, BP will return to levels similar to that before treatment with the medication, if all other factors remain the same. If antihypertensive therapy is to be terminated for some reason, the dosage should be gradually reduced, as abrupt withdrawal can cause rebound hypertension.

Side effects of antihypertensives are common. The most common side effect of antihypertensives is *hypotension*, especially postural hypotension. Another side effect common with many of the antihypertensives is *bradycardia*. An exception is hydralazine, which can cause tachycardia.

Thiazide Diuretics

Most patients meeting the criteria for drug therapy should be started on thiazide-type diuretics, either alone or in combination with a drug from one of the other drug classes: ACE inhibitors, ARBs, beta-blockers, or calcium channel blockers. Thiazide diuretics appear to be as effective and have fewer side effects compared to other antihypertensive agents and, in addition, are inexpensive.

Beta-Adrenergic and Calcium Channel Blockers

Like thiazide diuretics, beta-adrenergic blockers such as carvedilol (Coreg) and metoprolol (Lopressor, Toprol XL) are generally well tolerated and are suitable for initial therapy in some patients with angina, following myocardial infarction, ischemic heart disease, heart failure, and certain arrhythmias. Only bisoprolol, carvedilol, and metoprolol succinate (extended-release) have been proven to reduce mortality when used in patients with heart failure. Atenolol should not be used to treat hypertension because this drug has no effect in reducing cardiovascular events and mortality.

Calcium channel blockers such as diltiazem (Cardizem) and amlodipine (Norvasc) are an initial therapy option for hypertensive patients with diabetes or high coronary disease risk. Studies show they are more effective in treating African American patients, older adults, and patients with higher pretreatment blood pressure readings. They may also be preferred in patients with obstructive airways disease. Based on historical data, *short-acting* calcium channel blockers should never be used to manage *hypertensive crisis* because of the reports of increased risks of myocardial infarction and mortality.

ACE Inhibitors (ACEIs)

Another class of antihypertensives is the ACE inhibitors, for example, lisinopril or enalapril. Inhibition of ACE lowers blood pressure by *decreasing vasoconstriction*; there are not significant changes in heart rate or cardiac output. ACEIs are first- or second-line agents in the treatment of hypertension and are excellent alone, but also effective and synergistic in combination with other antihypertensives, including diuretics and calcium channel blockers.

ACEIs are especially good choices for patients who also have other serious conditions, including those with heart failure, following myocardial infarction, when high coronary disease risk exists, diabetes, renal disease, and cerebrovascular disease. For example, ACEIs can be considered drugs of choice for patients with high blood pressure and nephropathy because they slow the progression of the renal disease. They are more effective in younger and White populations and less effective in African American patients, unless given in higher doses or in combination with a diuretic.

Side effects of ACE inhibitors (infrequent and usually mild) can include:

- ❗ Rash or photosensitivity
- ❗ Hypotension
- ❗ Chronic dry cough or nasal congestion (resolved by switching to ARB class)
- ❗ Hyperkalemia (monitor serum potassium levels periodically)

Cautions or contraindications with ACE inhibitors apply to:

- Collagen disease, for example, lupus or scleroderma
- Heart failure
- Angioedema
- ❗ Pregnancy and lactation (contraindicated)

Interactions of ACE inhibitors apply to:

- Diuretics (potentiate hypotension; watch BP closely)
- Vasodilators (watch BP closely)
- Potassium-sparing diuretics and potassium supplements (hyperkalemia risk)
- Nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates (antagonize effects of ACE inhibitors and increase deterioration of renal function in patients with compromised renal function)
- Antacids (decrease absorption)
- Digoxin (possible digitalis toxicity)
- Lithium (risk of lithium toxicity)

Angiotensin Receptor Blockers (ARBs)

ARBs are similar to ACEIs and are generally used as alternatives. They block the angiotensin receptor that causes vasoconstriction when stimulated by angiotensin II. ARBs such as losartan (Cozaar) and valsartan (Diovan) block the effects of angiotensin II, decreasing blood pressure without a marked change in heart rate.

Compared to ACEIs, ARBs are associated with a lower incidence of drug-induced cough, rash, and/or taste disturbances and are used in those patients who cannot tolerate ACEIs. Like the ACEIs, African American patients experience a smaller antihypertensive response with the ARBs compared to other populations. The addition of a low-dose thiazide diuretic to an ARB significantly improves hypertensive efficacy. ARBs are also good choices for patients with other serious conditions, including those with heart failure, diabetes, and renal disease.

Side effects are relatively uncommon with ARBs and include dizziness, orthostatic hypotension, upper respiratory tract infections, and hyperkalemia.

Cautions or contraindications for ARBs apply to:

Renal impairment
Pregnancy and lactation
Children

Interactions with ARBs are similar to those experienced with ACEIs.

Other Antihypertensives

Antiadrenergic Agents

Clonidine (Catapres) is a *central-acting* alpha-adrenergic blocking agent, used mainly in the treatment of hypertension. It is available as an oral preparation, a transdermal system, and an injection for epidural use. Clonidine has also been used successfully in a variety of other conditions, including ADHD, nicotine/opiate withdrawal, vascular headaches, glaucoma, ulcerative colitis, Tourette's syndrome, and treatment of severe pain in cancer patients.

Prazosin (Minipress) is a *peripheral-acting* alpha-adrenergic blocker used primarily to treat hypertension. Other agents in this class are used to treat benign prostatic hyperplasia (BPH). Treatment with alpha-adrenergic blockers was once considered potentially favorable for the management of hypertension in patients with BPH to target both blood pressure and BPH symptoms. However, a study determined that patients treated with the alpha-blocker doxazosin, when compared with those treated with the diuretic chlorthalidone, had an increased risk for stroke and heart failure. Therefore, hypertension should not be managed with an alpha-blocker alone, and BPH symptoms should be managed separately.

Peripheral Vasodilator

Hydralazine, a peripheral vasodilator, is sometimes used in the treatment of moderate to severe hypertension, especially in patients with CHF, because it increases the heart rate and cardiac output. The drug is generally used in conjunction with a diuretic and another hypotensive agent, for example, a beta-blocker. A fixed-dose combination of isosorbide dinitrate and hydralazine (BiDil) is available for the treatment of heart failure.

Side effects of hydralazine can include:

❗ *Tachycardia* and palpitations
Headache and flushing
❗ Orthostatic hypotension
GI effects, including nausea, vomiting, diarrhea, and constipation
Blood abnormalities
❗ Edema and weight gain

Cautions or contraindications for hydralazine apply to:

Systemic lupus erythematosus (SLE)

Renal disease

Coronary artery disease and rheumatic heart disease

Pregnancy, usually (however, many regard hydralazine as the antihypertensive of choice during preeclampsia)

Figure 14-2 illustrates the various mechanisms to reduce blood pressure, and Table 14-2 provides a summary of the classifications and specific drug examples of antihypertensives.

Table 14-2 Antihypertensives

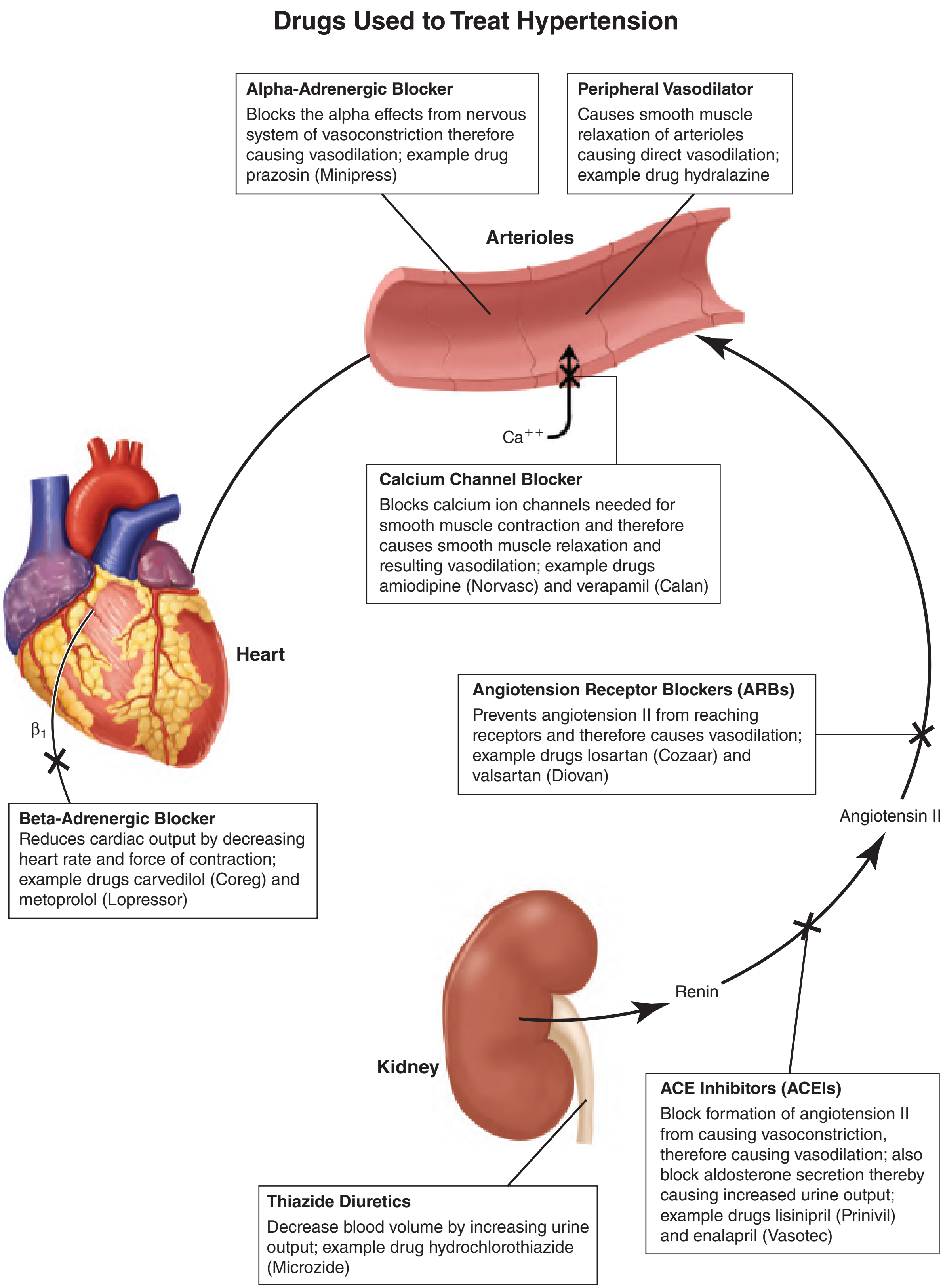
Generic Name	Trade Name	Dosage
Beta-Adrenergic Blockers		
Acebutolol	Sectral	400–1,200 mg PO daily divided into q12h dosing
Atenolol	Tenormin	25–100 mg PO daily
Betaxolol	Kerlone	5–20 mg PO daily
Bisoprolol	Zebeta	2.5–20 mg PO daily
bisoprolol/HCTZ	Ziac[a]	2.5/6.25 mg to 10/6.25 mg daily
Carvedilol	Coreg	6.25–25 mg PO bid with food (also has vasodilatory properties)
	Coreg CR	20–80 mg daily with food (SR)[a]
Labetalol	Trandate	100–400 mg PO q12h
metoprolol	Lopressor	100–400 mg PO daily in divided doses
metoprolol/HCTZ	Lopressor HCT[a]	50/25 mg to 100/50 mg PO daily
	Toprol XL	50–100 mg PO daily (SR)
Nadolol	Corgard	40–320 mg PO daily
Nebivolol	Bystolic	5–40 mg PO daily (also has vasodilatory properties)
Pindolol	Visken	5–30 mg PO q12h
Propranolol	Inderal	160–480 mg PO daily in two to three divided doses
	Inderal LA[a]	80–160 mg PO daily (SR)
sotalol	Betapace	160–320 mg PO daily in two to three divided doses
timolol	Blocadren	10–30 mg PO daily in two divided doses (max of 60 mg / day)

Generic Name	Trade Name	Dosage
Calcium Channel Blockers		
amlodipine[b]	Norvasc	2.5–10 mg PO daily
Diltiazem	(cap) Cardizem CD (tab) Cardizem LA	120–360 mg PO daily (SR); regular-release tabs are not approved to treat hypertension
	Diltiazem SR	120–180 mg PO bid (SR)
Nifedipine	Procardia XL Adalat CC	30–90 mg PO daily (SR)
Verapamil	Calan SR, Isoptin SR	120–240 mg PO one to two times per day (SR)
ACE Inhibitors		
benazepril[b]	Lotensin	10–20 mg PO one to two times per day
Captopril	Capoten	25–150 mg PO q8–12h
Enalapril	Vasotec	5–20 mg PO bid
lisinopril[b]	Prinivil, Zestril	5–40 mg PO daily
Ramipril	Altace	2.5–20 mg PO one to two divided doses
Trandolapril	Mavik	1–4 mg PO daily
Moexipril	Univasc	7.5–30 mg PO daily
ARBs		
losartan[b]	Cozaar	25–100 mg PO one to two divided doses
olmesartan[b]	Benicar	20–40 mg PO daily
Telmisartan	Micardis	20–80 mg PO daily
valsartan[b]	Diovan	80–320 mg PO daily
sacubitril/valsartan	Entresto	Indicated for heart failure only; available in three doses (24/26 mg, 49/51 mg, and 97/103 mg) taken PO bid
Other Antihypertensives		
Antiadrenergic Agents		
Clonidine	Catapres	0.1–1.2 mg PO daily in divided doses
	Catapres TTS	Weekly patch (delivers 0.1–0.3 mg/24 h)
prazosin	Minipres	1–20 mg PO daily in two to three divided doses
Peripheral Vasodilator		
Hydralazine		10–50 mg PO two to four times per day; IM, IV dose varies

[a] Combo medication consisting of two drug classes.

[b] Available in many combinations with drugs from other classes.

Note: This is only a representative list of the most commonly used drugs in this category. There are many others and many in combination with a diuretic. All extended-release products (ER/SR) must be swallowed intact! Quick release of the medication can cause the blood pressure to drop suddenly, sending the patient into shock. Caution is advised owing to potential confusion with various name extensions designating extended-release formulations (CC, CD, CR, LA, SR, and XL).



Drugs Used to Treat Hypertension

Alpha-Adrenergic Blocker
Blocks the alpha effects from nervous system of vasoconstriction therefore causing vasodilation; example drug prazosin (Minipress)

Peripheral Vasodilator
Causes smooth muscle relaxation of arterioles causing direct vasodilation; example drug hydralazine

Calcium Channel Blocker
Blocks calcium ion channels needed for smooth muscle contraction and therefore causes smooth muscle relaxation and resulting vasodilation; example drugs amiodipine (Norvasc) and verapamil (Calan)

Angiotension Receptor Blockers (ARBs)
Prevents angiotension II from reaching receptors and therefore causes vasodilation; example drugs losartan (Cozaar) and valsartan (Diovan)

Beta-Adrenergic Blocker
Reduces cardiac output by decreasing heart rate and force of contraction; example drugs carvedilol (Coreg) and metoprolol (Lopressor)

ACE Inhibitors (ACEIs)
Block formation of angiotension II from causing vasoconstriction, therefore causing vasodilation; also block aldosterone secretion thereby causing increased urine output; example drugs lisinipril (Prinivil) and enalapril (Vasotec)

Thiazide Diuretics
Decrease blood volume by increasing urine output; example drug hydrochlorothiazide (Microzide)

Figure 14-2 Various mechanisms of action of drugs used to treat hypertension.

Learning Hint

The ending of several drug names can help you determine their classification. Notice from Table 14-2 that all beta-adrenergic blockers end in *-lol*, all ACE inhibitors end in *-pril*, and all angiotension receptor blockers end in *-sartan*.

Patient Education

Patients taking antihypertensives should be instructed regarding:

- Routinely monitoring blood pressure at home, keeping a log of their blood pressure readings, and sharing this information with their physician
- Immediate reporting of any adverse side effects, especially slow or irregular heartbeat, dizziness, weakness, breathing difficulty, gastric distress, and numbness or swelling of extremities
- Taking the medication on time as prescribed by the physician; *not* skipping a dose or doubling a dose; *not* discontinuing the medicine, even if the patient is feeling well, without consulting the physician first
- Rising slowly from a reclining position to reduce feelings of lightheadedness
- Taking care in driving a car or operating machinery if the medication causes drowsiness (ask the physician, nurse, or pharmacist about the specific medication, because medicines differ and individual reactions differ; older people are more susceptible to this effect)
- Potentiation of adverse side effects by alcohol, especially dizziness, weakness, sleepiness, and confusion
- Reduction or cessation of smoking to help lower blood pressure
- Importance of lifestyle modifications, such as exercise, quitting smoking, limiting alcohol usage, and eating a healthy diet to help control blood pressure; following the physician's instructions regarding appropriate diet for the individual, which may include a low-salt or low-sodium or weight-reduction diet if indicated
- Avoiding hot tubs and hot showers, which may cause weakness or fainting
- Mild exercise on a regular basis as approved by the physician
- Always swallowing the extended-release products intact; quick release of the medication into the system can cause the blood pressure to drop suddenly, causing loss of consciousness and possible shock
- Avoiding grapefruit juice while taking calcium channel blockers, which can increase the risk of hypotension and other adverse cardiac effects

Coronary Vasodilators

Coronary vasodilators are used in the treatment of angina. When there is insufficient blood supply (**ischemia**) to a part of the heart, the result is acute pain. The most common form of angina is angina pectoris, chest pain resulting from decreased blood supply to the heart muscle. Obstruction or constriction of the coronary arteries, which supply the heart muscle with oxygenated blood, results in angina pectoris. Vasodilators are administered to dilate these blood vessels (thus increasing myocardial oxygen supply) and stop attacks of angina or reduce the frequency of angina when administered prophylactically. Coronary vasodilators used in the treatment and prophylactic management of angina include nitrates, beta-blockers, and calcium channel blockers.

The nitrates used most commonly for relief of acute angina pectoris, as well as for long-term prophylactic management, are nitroglycerin and isosorbide (e.g., Isordil, Imdur). Nitroglycerin is available in several forms and can be administered in sublingual tablets allowed to dissolve under the tongue or a sublingual spray for the relief of acute angina pectoris. If chest pain is not relieved or worsens 5 min after a dose, EMS should be alerted because unrelieved chest pain can indicate an acute myocardial infarction.

Guidelines recommend instructing a patient with a prior prescription for nitroglycerin to call 911 immediately if chest discomfort or pain is persistent or worsened

5 min after *one* dose of nitroglycerin. Self-treatment with nitrates has been identified as a factor resulting in delays in emergency evaluation.

Nitroglycerin is also available in timed-release capsules and tablets and in an injectable formulation. Nitroglycerin tablets and capsules must be stored *only in glass containers* with tight-fitting metal screw tops away from heat to retain potency. Impaired potency of the SL tablets can be detected by the patient if there is an absence of the tingling sensation under the tongue common to this form of administration.

For the long-term prophylactic management of angina pectoris, nitroglycerin is frequently applied topically as a transdermal system. One type of nitroglycerin that is absorbed through the skin is Nitro-Bid ointment, applied with an applicator-measuring (Appli-Ruler) paper. Usual dosage is 0.5–2 inches applied every 8 h. The ointment is spread lightly (not massaged or rubbed) over any hairless skin area, and the applicator paper is taped in place. Care must be taken to avoid touching the ointment when applying (accidental absorption through the skin of the fingers can cause headache). If nitroglycerin ointment is discontinued, the dose and frequency must be decreased gradually to prevent sudden withdrawal reactions.

Another topical nitroglycerin product, which has a longer action, is in transdermal form (e.g., Nitro-Dur). The skin patch is applied every 24 h (on in A.M./off 12 h later in the P.M.) to clean, dry, hairless areas of the upper arm or body. Do not apply below the elbow or knee. *The sites should be rotated* to avoid skin irritation, and raw, scarred, or callused areas should be avoided. Patch dosage varies widely, from 0.1 to 0.8 mg/h daily.

Another nitrate used for the acute relief of angina pectoris and for prophylactic long-term management is isosorbide. It is available in SL tablets, regular-release tablets, and timed-release capsules and tablets. When using long-acting nitrates, a 12–14 h nitrate-free interval between the last dose of the day and the first dose of the following day is recommended to lessen the risk of nitrate tolerance.

Side effects of the nitrates can include:

❗ Headache (usually diminishes over time; analgesics may be given to alleviate pain)

❗ Postural hypotension, including dizziness, weakness, and syncope (*patients should be sitting during the administration of fast-acting nitrates*)

Transient flushing

Rash and skin irritation with transdermal forms

❗ Blurred vision and dry mouth (discontinue the drug with these symptoms)

❗ Hypersensitivity reactions, enhanced by alcohol, including nausea, vomiting, diarrhea, cold sweats, tachycardia, and syncope

Cautions or contraindications for nitrates apply to:

Glaucoma

GI hypermotility or malabsorption (with timed-release forms)

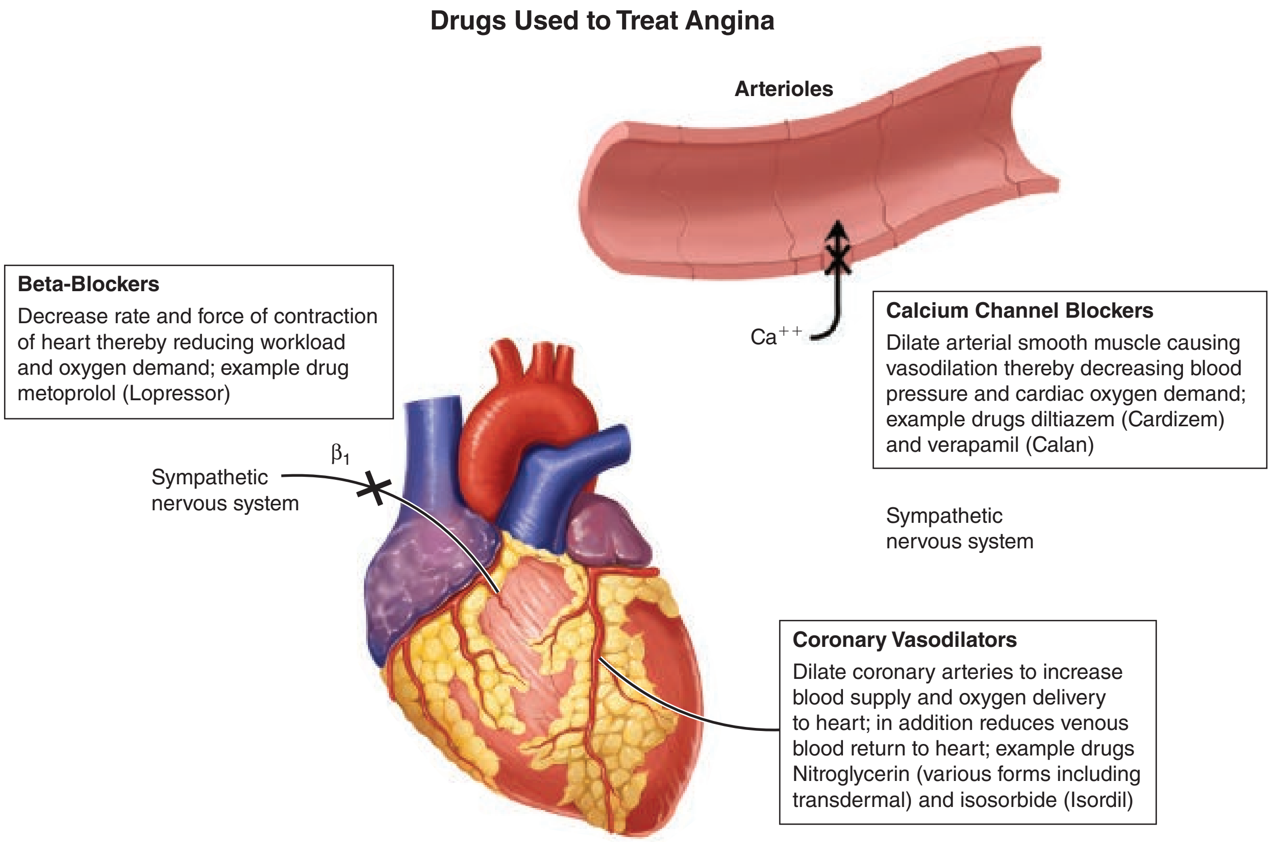
Intracranial pressure

Severe anemia

Hypotension

Interactions of nitrates may occur with alcohol, which potentiates hypotensive effects. Phosphodiesterase (PDE) inhibitors such as sildenafil (Viagra), used for erectile dysfunction, are contraindicated in men taking nitrates. The two drugs interact to cause a large, sudden, dangerous drop in blood pressure.

For the long-term prophylactic treatment of angina pectoris, beta-blockers such as metoprolol (Lopressor) and calcium channel blockers such as diltiazem (Cardizem) and verapamil (Calan) are frequently used (refer to the "Antiarrhythmic Agents" section in this chapter for information on side effects, etc.). Figure 14-3 illustrates drugs used to treat angina.


Drugs Used to Treat Angina
Arterioles
Ca^{++}
β_1
Sympathetic nervous system
Sympathetic nervous system

Beta-Blockers
Decrease rate and force of contraction of heart thereby reducing workload and oxygen demand; example drug metoprolol (Lopressor)

Calcium Channel Blockers
Dilate arterial smooth muscle causing vasodilation thereby decreasing blood pressure and cardiac oxygen demand; example drugs diltiazem (Cardizem) and verapamil (Calan)

Coronary Vasodilators
Dilate coronary arteries to increase blood supply and oxygen delivery to heart; in addition reduces venous blood return to heart; example drugs Nitroglycerin (various forms including transdermal) and isosorbide (Isordil)

Figure 14-3 Various mechanisms of action of drugs used to treat angina.

Patient Education

Patients receiving coronary vasodilators (nitrates) should be instructed regarding:

- Administering fast-acting preparations (sublingual tablets or spray) while sitting down because the patient may become lightheaded
- Rising slowly from a reclining position
- Not drinking alcohol or taking PDE inhibitors while taking these medicines, which can cause a serious drop in blood pressure
- Using timed-release capsules or tablets to prevent attacks (they work too slowly to help once an attack has started)

(*Continued*)

The fact that nitrates taken for chronic angina may require periods of drug-free intervals to avoid the development of nitrate tolerance and lessening of antianginal effects

Taking timed-release capsules or tablets on an empty stomach with a full glass of water

Allowing sublingual tablets to dissolve under the tongue or in the cheek pouch and not chewing or swallowing them

Repeating sublingual tablets or spray in 5–10 min for a maximum of three tablets or sprays (if no relief or worsening of chest pain occurs within 5 min after the first tablet, activate EMS, or if EMS is unavailable, report to the emergency department; for patients known to have frequent angina, physicians may provide individualized instructions for the use of SL nitroglycerin, based on the characteristics of the patient's angina, time course, and response to the treatment

Not discontinuing the medication suddenly if administered for several weeks (dosage must be reduced gradually under the physician's supervision)

Sensations to be expected, including facial flushing, headache for a short time, and lightheadedness upon rising too suddenly (if these symptoms persist or become more severe, or other symptoms occur, such as irregular heartbeat or blurred vision, notify the physician at once)

Preventing attacks of angina by administering a sublingual tablet or spray before physical exertion or emotional stress (it is preferable to avoid physical or emotional stress when possible)

Table 14-3 provides a summary of coronary vasodilators.

Table 14-3 Coronary Vasodilators

Generic Name	Trade Name	Dosage
Nitrates[a]		
nitroglycerin	Nitrostat tabs S.L.	1–3 tabs q5min × 3 max in 15 min PRN
	Nitrolingual spray	1–2 sprays (0.4–0.8 mg) SL q5min × 3 max in 15 min PRN
	caps E.R.	2.5–9 mg PO q8–12h
	Nitro-Bid oint 2%	1–2 inches q6–8h (while awake and at bedtime for a 10- to 12-h nitrate-free interval); *Note*: 1 g unit dose foilpac equiv to ~1″
	Nitro-Dur, Minitran	1 transdermal patch to deliver 0.1–0.8 mg/h daily, rotate site; on 12–14 h per off 10–12 h
	IV, premixed or sol for inj	IV dose varies
isosorbide dinitrate		SL 2.5–5 mg × 3 max in 15–30 min
	Isordil	Prophylactic PO 10–40 mg bid–tid (allow for a 14-h nitrate-free interval)
	Dilatrate (SR)	PO 40 mg one to two times per day (18-h nitrate-free interval recommended)
with hydralazine	BiDil	PO 1–2 tabs tid (for heart failure)
isosorbide mononitrate	Imdur (SR)	10–20 mg PO bid (7 h apart) or tid at 8 A.M., 1 P.M., and 6 P.M.
		30–120 mg PO one time per day

Note: Beta-blockers and calcium channel blockers are also administered prophylactically for angina pectoris and can be given concurrently with the nitrates.

[a] For the prevention and treatment of angina pectoris.

Antilipemic Agents

It is estimated that nearly 50% of Americans have elevated total blood cholesterol levels above 200 mg/dL—a key risk factor for **coronary heart disease (CHD)**. Cardiovascular disease is the leading cause of death for men and women in the United States (more deaths than cancer, diabetes, accidents, and chronic lung diseases combined). High cholesterol can lead to arterial blockage, hardening of the arteries, blood clots, heart attack, or stroke and may even play a role in dementia.

Lipoproteins are responsible for transporting cholesterol and other fats through the bloodstream. *Low-density lipoproteins* (LDLs; "bad cholesterol") carry the largest amount of the cholesterol in the blood and are responsible for transporting and depositing it in the arterial walls. *Very low-density lipoproteins* (VLDLs; triglycerides) are precursors of the LDL and compose the largest proportion of lipids in the diet, adipose tissue, and blood. Triglycerides (TGs) are a source of energy; excess dietary calories are converted to TGs and stored as fat in the adipose tissue for future energy needs. Excess TGs (greater than the normal 150 mg/dL level) can be an independent risk factor leading to atherosclerosis and CHD, as well as pancreatitis.

High-density lipoproteins (*HDLs*; "good cholesterol") help transport LDL cholesterol from the walls of the arteries through the bloodstream to the liver for excretion. An HDL level of below 40 mg/dL is considered low, and each 1 mg/dL increase in the HDL level is associated with a 6% lower risk of cardiovascular disease. LDL cholesterol is the primary target of treatment in clinical lipid management. The use of therapeutic lifestyle changes (TLCs), including LDL-lowering dietary management (e.g., restriction of saturated and trans fats or cholesterol intake, including fiber and soy protein in the diet), weight control, appropriate exercise, limiting alcohol intake, and smoking cessation, can achieve the therapeutic goal (LDL below 100 mg/dL) in many persons. If these measures are inadequate, drug therapy must be added. Drug therapy aimed at reducing cholesterol levels either reduces hepatic production or intestinal absorption of cholesterol. Six categories of **antilipemic agents** used to lower blood cholesterol levels are available: HMG-CoA reductase inhibitors (the *statins*), bile acid sequestrants, nicotinic acid (niacin), fibric acid derivatives, cholesterol absorption inhibitors, and omega-3 fatty acids. Statins are considered first-line therapy when medication intervention is required, while nicotinic acid formulations are rarely initiated due to their negative effects on the liver.

Statins

HMG-CoA reductase inhibitors (statins) inhibit the enzyme for cholesterol synthesis. These agents are the most potent lipid-lowering medications available for monotherapy and are considered to be the first choice in managing high cholesterol. Statins (e.g., atorvastatin—Lipitor; simvastatin—Zocor) have been shown to be very effective in lowering LDL levels (up to 60%) and are modestly effective in reducing TG levels and increasing HDL levels, thereby reducing cardiovascular morbidity and mortality. Statins are generally well tolerated.

Because HMG-CoA is most active at night when dietary intake is low, most statins are generally given at bedtime to provide optimal decreases in LDL levels. Because of their longer half-lives, atorvastatin and rosuvastatin can be given at the same time each day, any time of day. Previously, the maximum dose of simvastatin was reduced from 80 to 40 mg (if using it for less than 12 months) because of the increased risk of myopathy from the higher dose.

Side effects of statins include:

- ❗ Myalgia and muscle weakness (can try switching to a different statin if problematic)

- Rhabdomyolysis (destruction of the muscle tissue leading to renal failure; reported rarely)
- Elevated liver enzymes (the FDA recently revised statin labeling by removing the recommendation for periodic liver function tests; baseline tests are still suggested, but follow-up monitoring is necessary only if clinically indicated)

Cautions or contraindications for statins apply to:

Hepatic or renal disease

Existing myalgia or muscle weakness

Pregnancy and breast-feeding

Children

Already taking gemfibrozil or hepatitis C protease inhibitors, diagnosed with HIV (increased risk for myopathy and rhabdomyolysis)

Interactions of certain statins with amiodarone, dronedarone, immunosuppressive drugs, erythromycin, azole antifungals, diltiazem, verapamil, *grapefruit juice*, or other antilipemic drugs (fibrates and niacin) increase the risk of myopathy and renal failure. Recently, the maximum recommended dose for most statins, when taken with certain interacting drugs, was also reduced because of safety considerations.

Bile Acid Sequestrants

Cholestyramine (Questran) and colesevelam (WelChol), which are not absorbed from the GI tract, bind bile acids in the intestine, interrupting the process by which bile acids are returned to the liver for reuse. Because bile acids are formed from cholesterol, sequestrants reduce total body cholesterol. Bile acid sequestrants can be used as monotherapy when moderate reductions in LDL levels are required or as an add-on therapy to statins. They should not be used as a single agent in the presence of elevated TGs.

Clinical Application

While statins can be considered among the most important medications a patient takes, they are also some of the most likely to be discontinued or not taken correctly by patients. Proper adherence to statins plays a major role in the success of the therapy (lowering LDL). Many times patients will self-discontinue a statin due to myopathy (muscle aches/cramps) without informing their doctor. Patients should be counseled that myopathy is a possible side effect, and that it can usually be resolved by switching to a different statin, lowering the dose of the current statin, or switching antilipemic drug classes. Patients should never discontinue medication without discussing with their physician or pharmacist, so it is important that you inform them of the common side effects and how they can be resolved. With this information patients are more likely to discuss side effects with their physician.

Side effects of bile acid sequestrants include:

- Constipation, gas, cramps, heartburn, nausea, anorexia, abdominal pain, and bloating (occurs frequently and may affect compliance)

Colesevelam is administered at lower doses because of its higher bile-binding capacity and is associated with fewer GI adverse effects.

Cautions or contraindications for bile acid sequestrants apply to:

- Biliary cirrhosis and obstruction
- GI obstruction or fecal impaction

Interactions with bile acid sequestrants can reduce the absorption of many drugs, including antibiotics, cardiac glycosides, fat-soluble vitamins, thiazide diuretics, and thyroid hormones (administer at least 1h before or 4h after the bile acid sequestrants).

Nicotinic Acid (Niacin)

Nicotinic acid reduces the hepatic synthesis of TGs and inhibits the mobilization of free fatty acids from the peripheral tissues. It lowers total and LDL cholesterol and TG levels in the serum and also raises HDL cholesterol levels. Niacin is rarely initiated as new therapy for patients, due to hepatotoxicity associated with long-term use. While it is still commercially available, it is generally reserved for patients who cannot tolerate other antilipemic drug classes, or who have a history of success with this therapy.

Side effects of niacin can be troublesome and include:

- ❗ GI upset, dyspepsia (indigestion), blurred vision, and fatigue
- ❗ *Skin flushing*, itching, and irritation (more common with immediate-release preparations; pretreatment with aspirin or ibuprofen can diminish cutaneous reactions)
- Glucose intolerance and hyperuricemia (abnormal uric acid levels in blood) (higher doses)
- ❗ Hepatotoxicity (especially with sustained-release products; monitoring hepatic function is recommended for all niacin formulations)

Note

Regular- and extended-release formulations of niacin are not bioequivalent and are not interchangeable.

Cautions or contraindications of niacin include:

- Hepatic, gallbladder, or peptic ulcer disease; diabetes; glaucoma; or gout
- Pregnancy and lactation (high doses)
- Children (<10 years old)

Interactions of niacin occur with:

- Antihypertensives and vasodilators (potentiate hypotensive effects)
- Antidiabetic agents with the loss of blood glucose control
- Alcohol (worsens flushing)

Fibric Acid Derivatives (Fibrates)

The fibrates fenofibrate (TriCor) and gemfibrozil (Lopid) possess minimal LDL-reducing capacity but are especially effective in patients who have extremely high TG levels and elevated cholesterol levels, and in patients with combined forms of hyperlipidemia. They are a good choice for diabetics because they improve glucose tolerance. The mechanism by which fibrates reduce TGs is poorly understood. Fibrates may be used in combination with other antilipemics because these agents appear to be additive in lowering LDL and raising HDL cholesterol. Fibrates are generally well tolerated.

Side effects of fibrates can include:

- ❗ GI complaints (diarrhea, dyspepsia, nausea and vomiting, and abdominal pain)
- ❗ Cholethiasis (gallstones in the gallbladder) because of the increased biliary excretion of cholesterol, jaundice, blood dyscrasias, myopathy (abnormal condition of skeletal muscles)

Cautions or contraindications for fibrates apply to:

Gallbladder, hepatic, renal disease, or peptic ulcer

Pregnancy and lactation

Children

Interactions of fibrates occur with:

Oral anticoagulants and hypoglycemic agents (potentiate effects)

Statins to increase the risk of serious muscle problems and elevated liver enzymes (use together only in the lowest effective doses and if benefits outweigh risks)

Ezetimibe is not advised (increased risk of cholethiasis)

Cholesterol Absorption Inhibitor

Ezetimibe (Zetia) moderately reduces LDL levels by inhibiting intestinal absorption of both dietary and biliary cholesterol, blocking its transport in the small intestine. It can be taken simultaneously with a statin (Vytorin, a combination product), allowing for lower doses of the statin to be used, and the LDL-lowering effects of the two drugs are additive. Ezetimibe is generally well tolerated, with abdominal pain, back pain, and arthralgia being reported. Patients with gallbladder disease and moderate to severe hepatic insufficiency should not take it.

Administer ezetimibe at least 1–2 h before or 2–4 h after administering antacids and bile acid sequestrants, respectively. Avoid use with cyclosporine (increases serum concentrations of both drugs) and fibrates (increased risk of cholethiasis).

Omega-3 Fatty Acids

Omega-3 fatty acids include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), found in fatty cold-water fish, and alpha-linolenic acid (ALA), found in flaxseed, tofu, soybean oil, canola oil, and nuts. There is evidence that EPA and DHA may have a role in the prevention of primary and secondary heart disease and reduce TGs (as an adjunct to diet or simvastatin).

The best source of omega-3 fatty acids is fatty fish, like salmon, but fish oil capsules may be more convenient, especially if high doses are needed. A highly concentrated and purified form of omega-3 fatty acids is also available by prescription only as *Lovaza*. Fish oil can cause nausea, heartburn, or diarrhea. A fishy aftertaste can be reduced by refrigeration or freezing (Lovaza should not be frozen). Because omega-3 fatty acids inhibit platelet aggregation, caution is advised when used concurrently with anticoagulants, platelet inhibitors, and thrombolytic agents.

The DHA component of omega-3 fatty acids may be responsible for the elevations in LDL levels experienced with these products; patients should be monitored to ensure their LDL levels do not increase excessively.

Table 14-4 provides a summary of antilipemic agents.

Table 14-4 Antilipemic Agents

Generic Name	Trade Name	Dosage
Antilipemic Agents		
Statins		
atorvastatin	Lipitor	10–80 mg PO daily
fluvastatin	Lescol Lescol XL	20–80 mg PO daily
lovastatin	Mevacor	20–80 mg PO at bedtime with food
pitavastatin	Livalo	1–4 mg PO qd
pravastatin	Pravachol	10–80 mg PO at bedtime
rosuvastatin	Crestor	5–40 mg PO daily
simvastatin	Zocor	5–40 mg PO at bedtime (80 mg if already on it with no evidence of myopathy)
Bile Acid Sequestrants		
cholestyramine	Questran, Questran Light	4 g one to two times per day ac; mix powder with water, milk, or juice
colesevelam	Welchol	6 tabs (625 mg each) daily or 3 tabs bid with food and a full glass of water; max 7 tabs per day
Nicotinic Acid		
niacin	Niaspan (Rx) Slo-Niacin (OTC)	Dose varies with response; take after meals or a snack
Fibric Acid Derivatives		
fenofibrate	Antara, Lofibra, Tricor, Trilipix	43–200 mg PO daily with food depending on formulation/manufacturer
gemfibrozil	Lopid	600 mg PO bid ac
Cholesterol Absorption Inhibitor		
ezetimibe	Zetia	10 mg PO daily
Omega-3 Fatty Acids		
fish oil (OTC)	Lovaza (Rx)	3–6 g per day 4 g per day
Combinations		
atorvastatin/amlodipine	Caduet	PO daily; dose varies with response
ezetimibe/simvastatin	Vytorin	PO daily evening; dose varies with response

Note: Other antilipemic agents are available. Some reduce triglycerides as well.

Patient Education

Patients on antilipemic therapy should be instructed regarding:

- Continuing diet (low-fat, low-cholesterol) and aerobic exercise
- Taking the medicine with meals to reduce GI upset
- Reporting side effects to the physician immediately, *especially muscle pain, tenderness, weakness, dark-stained urine, or bleeding*
- With cholestyramine, the importance of a high-fiber diet and/or a stool softener, fat-soluble vitamin and folic acid supplements, and not taking other medication within 4 h
- Expecting facial flushing with niacin (unless extended-release formula is used)
- Taking most statins in the evening (the body synthesizes most cholesterol at night)
- *Avoiding grapefruit juice* while taking statins; adverse effects are potentiated
- Giving their health care professional a list of all the medicines, herbs, nonprescription drugs, or dietary supplements they are taking so that potential interactions can be identified
- The importance of initial liver function tests
- If all the other factors remain the same, the medication will probably need to be taken throughout the patient's lifetime; sometimes diet and exercise will eliminate the need

Antithrombotic Agents

Blood normally has the ability to flow freely through blood vessels, yet clot when the need arises. Normal hemostasis or blood coagulation involves the formation of a fibrin clot or thrombus so a minor cut would not cause us to bleed profusely. However, inappropriate thrombus formation can be caused by vessel-wall injury, circulatory stasis, increased blood coagulability, immobilization, obesity, cigarette smoking, medication therapy, and other factors. The inappropriate thrombus formation or clot can dislodge and travel through the bloodstream (thromboembolism or TE), where it can fully or partially obstruct blood flow, leading to tissue damage. **Antithrombotic agents**, which interfere with or prevent thrombosis or blood coagulation, include anticoagulants, platelet inhibitors, and thrombolytics.

Anticoagulants

Anticoagulants prevent the formation of the fibrin clot by interfering with one of the steps leading to fibrin formation. They are divided into two general groups: oral (coumarin derivatives and the new oral anticoagulants) and injectable (heparins). The action of these two classes is quite different. However, their purpose is the same: to prevent the formation of clots or decrease the extension of existing clots in such conditions as venous thrombosis, stroke, pulmonary embolism, and coronary artery occlusion. Also, many patients with artificial heart valves, mitral valve disease, or chronic atrial fibrillation, or postsurgical patients (cardiac bypass, vascular surgery, and hip or knee replacement) receive anticoagulants to prevent embolism or thrombosis. Patients on anticoagulants, especially older patients, should be constantly observed for *bleeding complications*, such as cerebrovascular accidents (CVAs). The coumarin derivatives (warfarin) and heparin do not dissolve existing clots; they only interfere with the coagulation process, preventing clot formation and/or propagation.

Warfarin

Warfarin (Coumadin) is administered *orally* (it is also available as an injectable preparation, which is rarely used). This medicine alters the synthesis of blood coagulation factors in the liver by interfering with the action of vitamin K. The *antidote* *for serious bleeding complications during warfarin therapy is prothrombin complex concentrate or fresh frozen plasma and vitamin K*. The action of warfarin is slower than that of heparin; therefore, warfarin is generally used as follow-up for long-term anticoagulant therapy, although warfarin may be started at the same time as heparin.

The most commonly used laboratory method of monitoring therapy with warfarin is the international normalized ratio (INR). The INR serves as a guide in determining the dosage. Dose adjustments made are based on INR and vary from patient to patient. For most patients taking warfarin an INR of 2.0–3.0 sec is desirable, although for higher-risk patients the range raises to 2.5–3.5 sec. It is important when adjusting the dose to allow 3–5 days for the INR to adjust before making another dosing change.

Interactions of warfarin with *many* drugs have been reported. Concurrent administration of any other drug should be investigated, and the following drugs should be *avoided* if possible. Some of the drugs that may *increase* response to warfarin include:

Anabolic steroids
Alcohol (acute intoxication)
Proton pump inhibitors
All NSAIDs, including aspirin; thrombolytics
Tricyclic antidepressants; SSRIs
Thyroid drugs
Amiodarone, propafenone, and quinidine
Many anti-infective agents
Many antilipemic agents
Acetaminophen (large daily doses or long duration)
Grapefruit juice, fish oil, vitamin E, many herbal supplements

Some of the drugs that may *decrease* response to warfarin include:

Alcohol (chronic alcoholism)
Barbiturates
Estrogen (including oral contraceptives)
Antiretroviral protease inhibitors

Additionally, foods that are naturally high in vitamin K (leafy green vegetables), should be eaten by patients on warfarin with consistency, meaning eating approximately the same amount of these types of food each day. There are many other interactions with warfarin. Always check before administering any other medicine.

New Oral Anticoagulants

Although warfarin was the mainstay of oral anticoagulation therapy for over 50 years, its significant limitations and interactions have led to research and the development of acceptable alternatives. In October 2009, dabigatran (Pradaxa) was the first oral anticoagulant (direct thrombin inhibitor) to be approved by the FDA in more than half a century. This was followed by the approval of two more oral anticoagulants (factor Xa inhibitors)—rivaroxaban (Xarelto) and apixaban (Eliquis), and most recently, edoxaban (Lixiana).

Compared to warfarin, the new oral anticoagulants have a rapid onset and predictable anticoagulant effects and fewer food and drug interactions; routine laboratory monitoring is not required.

However, anticoagulant effects cannot be monitored with standard laboratory testing, and there is currently no reversal agent in case of uncontrolled major bleeding or the need for emergency surgery (although some are in early clinical trials).

Dabigatran, rivaroxaban, apixaban, and edoxaban are all indicated for reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Rivaroxaban and edoxaban are also indicated for venous thromboembolism prevention, post-hip or -knee replacement, and deep vein thrombosis/pulmonary embolism (DVT/PE) treatment or prevention of recurrence.

Heparin and Low-Molecular-Weight Heparins

There are two types of heparin: the standard or unfractionated type (UFH) and the low-molecular-weight heparins (LMWHs).

Heparin is not absorbed from the GI tract, and the standard type (UFH) must be administered *intravenously* or *subcutaneously*. The LMWH type is usually only administered subcutaneously but may be given IV as well. Heparin acts on thrombin, inhibiting the action of fibrin in clot formation. The *antidote for serious bleeding complications during heparin therapy is protamine sulfate*. When administered IV, the action of heparin is immediate. A *dilute flushing* solution of heparin is also used to maintain the patency of indwelling venipuncture devices used to obtain blood specimens and of catheters used for arterial access (arterial lines). *Be sure to check that it is a dilute flushing solution before injection, and not full-strength heparin.* However, 0.9% sodium chloride (normal saline) injection alone is used to flush *peripheral* venipuncture devices, for example, PRN adapters. Heparin is *not* normally used to flush these devices because of possible drug incompatibilities and laboratory test interferences.

The LMWHs include enoxaparin (Lovenox) and dalteparin (Fragmin). When administered subcutaneously, monitoring of anticoagulant effect is not necessary, but periodic complete blood counts (CBCs), stool occult blood tests, and platelet counts are recommended during treatment.

Unlike UFH, in the case of clinically significant bleeding, no agent fully reverses the activity of the LMWHs, although protamine has some activity and should be given for life-threatening bleeding along with packed red blood cells and fresh frozen plasma transfusions if indicated. Fondaparinux (Arixtra), a closely related pentasaccharide, is not generally classified as an LMWH. It is an indirect clotting factor Xa inhibitor and lacks a specific antidote in the event of excessive anticoagulation.

Enoxaparin was the first LMWH to be approved in the United States. It is currently approved for the prevention of deep vein thrombosis (DVT) in patients undergoing hip or knee replacement or abdominal surgery, for the treatment of unstable angina and ST-elevation myocardial infarction (STEMI), and for the inpatient treatment of acute DVT and pulmonary embolism (PE). It is also used in the outpatient treatment of acute DVT not associated with pulmonary embolism and is combined with warfarin (until INR reaches 2–3 sec).

When heparin is administered subcutaneously, especially if the patient is discharged and the medication will be administered at home, be sure to stress *patient education*.

The activated partial thromboplastin time (aPTT) is the most common laboratory test for monitoring heparin therapy. When long-term anticoagulant therapy is begun with warfarin, there is a short-term overlap period in which both heparin and warfarin are administered concurrently.

Interactions of all anticoagulants with other anticoagulants, for example, aspirin and NSAIDs, platelet inhibitors, and fish oil, or with thrombolytic agents, for example, alteplase (tPA), may increase the risk of hemorrhage.

Side effects of all anticoagulants can include:

- ❗ Major hemorrhage
- ❗ Thrombocytopenia
- ❗ Minor bleeding (e.g., petechiae, nosebleed, and bruising)
- ❗ Blood in the urine (hematuria) or stools (melena)
- ❗ Osteoporosis with long-term heparin use (less with the LMWHs; none with the other agents)

Cautions or contraindications for anticoagulants apply to:

GI disorders and ulceration of GI tract
Hepatic and renal dysfunction
Blood dyscrasias
Pregnancy (heparin can be used with caution as it does not cross the placenta)
Stroke (may increase the risk of fatal cerebral hemorrhage after stroke)
Patients with prosthetic heart valves (with the new oral anticoagulants)
Lumbar puncture and epidural anesthesia (could result in paralysis)

Table 14-5 provides a summary of the anticoagulants.

Table 14-5 Anticoagulants

Generic Name	Trade Name	Dosage
Anticoagulants, Oral		
Coumarin Derivative		
Warfarin	Coumadin, Jantoven	PO dose varies, based on PT/INR results; initial starting dose for most adults is 5 mg daily
Factor Xa Inhibitors		
apixaban	Eliquis	PO 2.5–5 mg two times per day
rivaroxaban	Xarelto	PO 20 mg one time daily with P.M. meal (stroke prevention) PO 15 mg two times daily for 3 weeks, and then 20 mg one time daily with food (DVT/PE treatment or prevention) PO 10 mg once daily for 35 days (post-hip replacement) PO 10 mg one time daily for 12 days (post-knee replacement)
edoxaban	Lixiana	PO 60 mg daily (stroke prevention) PO 30-60 mg daily (DVT or PE Treatment)

(*Continued*)

Table 14-5 Anticoagulants (*Continued*)

Generic Name	Trade Name	Dosage
Thrombin Inhibitor		
dabigatran	Pradaxa	PO 150 mg two times daily (75 mg for creatinine clearance 15–30 mL/min); store in original container only up to 4 months
Anticoagulants, Injectable		
Unfractionated Heparin		
heparin		IV, SQ dose varies
Low-Molecular-Weight Heparins		
dalteparin	Fragmin	SQ, in fixed or body-weight-adjusted doses one to two times daily
enoxaparin	Lovenox	One to two times daily SQ dose and duration varies; reduce dose for creatinine clearance <30 mL/min
Factor Xa Inhibitor		
fondaparinux	Arixtra	Daily subcutaneous dose varies; closely related to the LMWHs

Note: This is a representative sample; many other products are available.

Patient Education

It is *very important* that patients on anticoagulant therapy be instructed regarding:

- Reading the FDA-approved medication guide dispensed with the oral anticoagulants
- Importance of compliance with taking medications as prescribed and required laboratory monitoring (if any)
- The fact that this medication does not dissolve clots and that it decreases the clotting ability of the blood and helps prevent the formation of harmful blood clots in the blood vessels and heart
- Taking the medication as prescribed at the same time every day
- Not changing brands of the medication without the physician's approval
- Avoiding eating large amounts of grapefruit or drinking grapefruit juice or cranberry juice
- Avoiding shots such as flu shots, shingle vaccine, and pneumonia vaccine (talk with your health care professional before getting shots)
- Avoiding activities and contact sports that may cause injury, cuts, or bruises
- Using a soft toothbrush and an electric razor to prevent cuts while shaving
- Always wearing closed-toe shoes
- Using a night light to prevent falls
- Immediately reporting unusual bleeding, bruising, brown spots, blood-tinged secretions, injury, trauma, dizziness, abdominal pain or swelling, back pain, headaches, and joint pain and swelling to their physician
- If prescribed, carrying vitamin K for emergency use
- Using a reliable birth control method
- Reporting allergic reactions such as skin rash to their physicians
- Avoiding smoking, the use of alcohol, and OTC medications
- Wearing identification and alerts at all times
- Keeping all follow-up appointments with their physician for laboratory work and for needed dosage changes

Note: Large amounts of vitamin K-rich foods can counteract warfarin therapy. Be consistent with your intake of foods high in vitamin K such as asparagus, broccoli, cabbage, Brussels sprouts, spinach, turnips, dried fruits, bananas, potatoes, peaches, and tomatoes to ensure a stable INR.

Platelet Inhibitor Therapy

Antiplatelet agents inhibit the aggregation (clumping) and release of thromboplastin from the platelets to begin the clotting process. **Platelet inhibitors** utilize a variety of mechanisms to interfere with activation pathways to prevent platelet clumping and are given as prophylactic therapy or as secondary prevention in patients with a history of recent stroke, recent MI, or established peripheral vascular disease. They are also used in the pharmacologic management of post-acute coronary syndrome (ACS), a spectrum of clinical conditions ranging from unstable angina to acute myocardial infarction, with or without ST-segment elevation. Platelet inhibitors are also used prior to and following percutaneous coronary intervention (PCI) with coronary stenting to prevent stent thrombosis.

In addition to drug therapy, patients should be educated on modifying risk factors for CHD and stroke, that is, abstinence from all forms of tobacco, weight control, low-fat and low-cholesterol diet, and aerobic exercise on a regular basis.

Dipyridamole (Persantine)

Dipyridamole (Persantine) is a non-nitrate coronary vasodilator that inhibits platelet aggregation. When used alone, it is ineffective as an antithrombotic for patients with DVT or transient ischemic attacks (TIAs) and therefore must be combined with other anticoagulant drugs. Dipyridamole is used in combination with aspirin in the prevention of ischemic stroke.

Side effects of dipyridamole, usually transient, can include:

Headache, dizziness, and weakness
Nausea, vomiting, and diarrhea
Flushing and rash

Caution with older adults (more susceptible to orthostatic hypotension).

A combination of low-dose aspirin with extended-release dipyridamole (Aggrenox) is approved for stroke prophylaxis. Most adverse effects are mild and similar to those with either agent alone.

Aspirin

Because of its ability to inhibit platelet aggregation, aspirin has been studied extensively for use in the prevention of thrombosis. Aspirin therapy, usually 75–325 mg daily, has been used after myocardial infarction or recurrent TIAs to reduce the risk of recurrence. Aspirin has also been used to reduce the risk of myocardial infarction in patients with unstable angina.

Aspirin therapy is not recommended for low-risk patients because of an increased risk of hemorrhagic stroke associated with long-term aspirin therapy. Patients should be instructed not to start aspirin therapy without consulting a physician first. Because of *gastric irritation*, aspirin should be administered with food or milk. Film-coated tablets, enteric-coated tablets, and buffered aspirin preparations are available to reduce gastric irritation. Aspirin is *contraindicated* for anyone with bleeding disorders.

Adenosine Diphosphate (ADP) Receptor Antagonists

ADP receptor antagonists block the activation of the platelet's receptor surface, thereby inhibiting platelet activation. Clopidogrel (Plavix) was the first agent approved in this class. It is used to reduce atherosclerotic events (myocardial infarction, stroke, and vascular death) in patients with a history of recent stroke, recent MI, or established peripheral vascular disease.

Clopidogrel is also used in combination with aspirin to prevent thrombosis of stents that are used to prop open diseased coronary arteries. Prasugrel (Effient) is a more potent antiplatelet agent with no clinically significant drug interactions identified to date.

The newest agent in this class, ticagrelor (Brilinta), is the first reversible oral ADP receptor antagonist. Its quicker onset of antiplatelet activity allows the platelet function to return to baseline more quickly and may result in fewer coronary artery bypass surgery-related bleeding events in patients requiring emergent intervention. Ticagrelor's shorter half-life necessitates twice-daily dosing compared with once-daily dosing of clopidogrel and prasugrel. Ticagrelor is contraindicated in severe hepatic impairment.

All ADP receptor antagonists are ***contraindicated*** in patients with active pathological bleeding (such as peptic ulcer) or a history of intracranial hemorrhage. ***Interactions*** of all platelet inhibitors with other anticoagulants, for example, aspirin and NSAIDs, other platelet inhibitors, or thrombolytic agents, may increase the risk of bleeding.

The use of certain PPIs (esomeprazole, omeprazole, including Prilosec OTC), azole antifungals, most macrolide antibiotics (except azithromycin), certain SSRIs (fluoxetine, fluvoxamine), and HIV NNRTIs may make clopidogrel less effective by inhibiting the enzyme that converts clopidogrel to the active form of the drug. The plasma concentrations of ticagrelor may be elevated by azole antifungals, HIV protease inhibitors, and some macrolide antibiotics; they may be reduced by carbamazepine, phenobarbital, phenytoin, and rifampin. Ticagrelor can increase digoxin concentrations (monitor levels) and increase lovastatin and simvastatin concentrations (avoid doses >40 mg).

Thrombolytic Agents

The body maintains a process to dissolve clots (fibrinolysis) after they have formed. Tissue plasminogen activator (t-PA) is a natural peptide that initiates fibrinolysis. **Thrombolytic agents** actually dissolve and liquefy the fibrin of the existing clot. Thrombolytic drugs (e.g., reteplase and alteplase) potentiate t-PA, resulting in clot dissolution, reperfusion of organs, and restoration of blood flow to tissues.

Thrombolytic agents, given IV, reduce mortality when used as early as possible but within the first 12 h after the onset of acute STEMI. Alteplase is also used to treat acute ischemic stroke (within 3–4.5 h of the onset of stroke symptoms) and acute pulmonary embolism. Administered in an ED or ICU setting, close monitoring of hemodynamics and vital signs is generally considered standard with thrombolytic therapy, particularly during the initial 24–48 h.

Intracranial hemorrhage is the most serious complication of thrombolytic therapy, but bleeding can occur at any site in the body. Bleeding occurs most commonly at access sites such as catheter insertion sites or venipuncture sites. Patients with preexisting coagulation problems, uncontrolled hypertension, severe chronic heart failure, and recent stroke are at the highest risk for developing bleeding complications during thrombolytic therapy.

Hemorrhage can result from concomitant therapy with heparin or other platelet-aggregation inhibitors. If severe bleeding occurs during therapy, the drug should be discontinued promptly. Rapid coronary lysis can result in the development of arrhythmias; however, they are generally transient in nature.

Hematopoietic Agents

Hematopoiesis is the formation, differentiation, and maturation of blood cells into specific cell lines. Hematopoietic agents to be discussed here include erythropoiesis-stimulating agents and the colony-stimulating factors. All hematopoietic agents are products of recombinant technology.

Erythropoiesis-Stimulating Agents

The erythropoiesis-stimulating agents (ESAs) such as epoetin alfa (Epogen or Procrit) are responsible for the regulation of the production and development of blood cells, normally in the bone marrow. Epoetin alfa stimulates the bone marrow to produce more red blood cells and is approved for the treatment of anemia in chronic renal failure, HIV infection, and anemia associated with chemotherapy. It also reduces the need for blood transfusions in anemic patients scheduled to undergo certain kinds of surgery. Darbepoetin alfa (Aranesp) is a *second-generation* agent that is dosed less frequently than epoetin alfa.

Before initiating ESA therapy, supplemental iron (folic acid, and/or vitamin B_{12} if necessary) is usually needed because adequate iron stores are necessary to incorporate iron into hemoglobin. Treatment of iron deficiency by regular use of iron improves erythropoiesis and response to ESA therapy. As of March 2010, prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology Program to prescribe and/or dispense epoetin alfa to patients with cancer. Recently, the FDA once again updated safety information in the black box warning regarding the use of ESAs: Use the lowest dose possible to gradually increase the hemoglobin (Hgb) concentration to avoid the need for transfusion.

Side effects of epoetin alfa (Epogen) include:

- ❗ Hypertension (especially in patients receiving dialysis)
- ❗ Flu-like symptoms
- GI effects
- Rash
- Chest pain
- ❗ Increased mortality, MI, stroke, thrombosis of vascular access, venous thromboembolic events, and increased risk of tumor progression or recurrence

Colony Stimulating Factors (CSFs)

A granulocyte colony-stimulating factor (G-CSF), filgrastim (Neupogen) is involved in the regulation and production of neutrophils in response to host defense needs. It lessens the severity of myelosuppression in patients with cancer and has allowed chemotherapy dose intensification or maintenance of dose intensity. *Use with caution in patients with sickle cell disorders.*

Side effects of filgrastim include:

- Bone pain (common)
- Headache
- Dermatological reactions

Table 14-6 provides a summary of platelet inhibitors, thrombolytic agents, and hematopoetic agents.

Table 14-6 Platelet Inhibitors, Thrombolytic Agents, and Hematopoetic Agents

Generic Name	Trade Name	Dosage
Platelet Inhibitors		
aspirin	Ecotrin, Ascriptin, others	75–325 mg PO daily
dipyridamole	Persantine	75–100 mg PO four times per day with warfarin or aspirin depending on indication
dipyridamole with aspirin	Aggrenox	1 cap PO bid
ADP Receptor Antagonists		
clopidogrel	Plavix	75 mg PO daily with or without food; 300 mg loading dose in ACS, usually with low-dose aspirin
prasugrel	Effient	60 mg PO loading dose and then 10 mg daily (5 mg if <60 kg) with aspirin for ACS managed with PCI
ticagrelor	Brilinta	180 mg PO loading dose and then 90 mg twice daily with aspirin (100 mg max) for ACS
Thrombolytic Agents		
alteplase, tPA	Activase	IV bolus and then IV infusion
	Cathflo Activase	2 mg injection one time (MR in 2 h) for IV catheter occlusions
reteplase, r-PA	Retavase	IV bolus two times (30 min apart)
tenecteplase, TNK-tPA	TNKase	Rapid IV bolus
Hematopoetic Agents		
ESAs		
darbepoetin alfa	Aranesp	IV, subcutaneous dose varies
epoetin alfa	Epogen, Procrit	IV, subcutaneous dose varies
CSFs		
filgrastim, G-CSF	Neupogen	IV, subcutaneous dose varies
pegfilgrastim (long acting filgrastim)	Neulasta	SC, 6 mg once per chemotherapy cycle

Note: This is a representative sample; other products are available.

Case Study A

Cardiovascular Drugs

A 77-year-old patient with heart failure has been treated successfully with a combination of ACE inhibitors and diuretics. However, the patient's symptoms worsened and became life-threatening despite pharmacologic treatment, so they are hospitalized for evaluation and stabilization on a cardiac glycoside.

1. How will the cardiac glycoside act to lessen the patient's heart failure?
   a. by increasing the patient's heart rate
   b. by increasing the force of cardiac contraction
   c. by increasing the patient's oxygen utilization
   d. by suppressing possible cardiac arrhythmias

2. What type of cardiac glycoside is the patient's physician most likely to prescribe?
   a. synthetic adenosine
   b. lidocaine or a related drug
   c. digitalis product
   d. thiazide

3. The physician alerts the patient that cardiac glycosides should be avoided if they have which of the following conditions?
   a. hyperthyroidism
   b. hyperkalemia
   c. hypermagnesemia
   d. impaired renal function

4. The patient should be advised to avoid certain medications because these can potentiate digoxin toxicity. Which of the following are in this category?
   a. cholestyramine, neomycin, and rifampin
   b. diuretics, calcium, and corticosteroids
   c. macrolides and antiarrhythmics
   d. adrenergics

5. If the patient is experiencing digoxin toxicity, what should be administered as an antidote?
   a. There is no antidote; just discontinue digoxin.
   b. Administer atropine
   c. Administer magnesium and calcium binders
   d. Administer digoxin-specific Fab fragments

Case Study B

Cardiovascular Drugs

A 37-year-old African American patient has been diagnosed with hypertension. The patient's physician discusses various options for pharmacologic treatment.

1. Regardless of race or age, what class of drugs is most commonly prescribed as first-line therapy in patients with hypertension?
   a. thiazides
   b. beta-blockers
   c. ACE inhibitors
   d. calcium channel blockers

2. What antihypertensives are known to be *more* effective in African American individuals and older adults?
   a. thiazides
   b. angiotensin receptor blockers
   c. nonthiazide diuretics
   d. calcium channel blockers

3. What antihypertensives are known to be less effective in African American individuals than in other groups?
   a. beta-adrenergic blockers
   b. antiadrenergics
   c. ACE inhibitors
   d. peripheral vasodilators

4. The patient also has lupus. What class of antihypertensive should be avoided?
   a. beta-adrenergic blockers
   b. antiadrenergics
   c. ACE inhibitors
   d. Thiazides

5. Suppose the patient is pregnant and experiences preeclampsia. Under this circumstance, the antihypertensive of choice would likely be
   a. chlorthalidone
   b. hydralazine
   c. losartan
   d. enalapril

Chapter Review Quiz

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication

1. ______ Isosorbide
2. ______ Zetia
3. ______ Lovenox
4. ______ Cardizem
5. ______ Zocor
6. ______ Plavix
7. ______ Crestor
8. ______ Hydralazine
9. ______ Quinidine
10. ______ Procainamide

Classification

a. Elevated cholesterol
b. Hypertension
c. Angina
d. Pulmonary emboli
e. Cardiac arrhythmia
f. Stroke prevention (platelet inhibitor)

Choose the correct answer.

11. In addition to the over 120 million adults in the United States that have hypertension, how many are suspected to have prehypertension?

a. 59 million
b. 17 million
c. 47 million
d. less than 1 million

12. Fibrillation refers to

a. rapid heartbeat
b. irregular heartbeat
c. slow heartbeat
d. insufficient heartbeat

13. Most drugs given to counteract arrhythmias have the potential for

a. causing hypertensive crisis
b. deranging calcium levels
c. slowing the heart rate
d. increasing glucose metabolism

14. Which of the following is especially important to monitor in patients receiving antiarrhythmic drugs?

a. electrolytes
b. glucose
c. platelets
d. lipids

15. Which of the following has been widely accepted as the most effective treatment for patients with life-threatening ventricular tachycardia or fibrillation?

a. insertion of an ICD
b. amiodarone
c. adenosine
d. propranolol

16. Inhibition of ACE lowers blood pressure by

a. decreasing cardiac output
b. increasing cardiac output
c. decreasing vasoconstriction
d. increasing vasoconstriction

17. Side effects from beta-blockers are most common in

a. patients of age 50 or younger
b. patients receiving IV administration of the drug
c. patients with preexisting arrhythmia
d. patients who experience migraines

18. Which of the following beta-blockers is considered to be selective?

a. metoprolol
b. propranolol
c. carvedilol
d. labetalol

19. Coronary vasodilators are used for the

a. treatment of hypotension
b. reduction of intracranial pressure
c. prevention of tachycardia and resulting syncope
d. treatment of angina

20. What antilipemic agent class is most commonly used to treat hyperlipidemia?

a. statins (HMG-CoA reductase inhibitors)
b. nicotinic acid derivatives
c. bile acid sequestrants
d. omega-3 fish oils

21. Increased risk of new-onset diabetes mellitus is most associated with high doses of

a. statins
b. cardiac glycosides
c. calcium channel blockers
d. bile acid sequestrants

22. Which drug is *least* effective in reducing the mortality associated with heart failure?

a. metoprolol succinate
b. atenolol
c. bisoprolol
d. carvedilol

23. What is one purpose of international normalized ratio (INR) monitoring?

a. to monitor warfarin therapy
b. to monitor kidney function for persons on antilipemics
c. to determine the need for pharmacologic treatment of angina
d. to determine the effectiveness of antihypertensives

24. How are low-molecular-weight heparins usually administered?

a. orally

b. sublingually

c. subcutaneously

d. as a skin patch

25. What is an advantage of the new oral anticoagulants?

a. slow onset for long-term therapy

b. fewer food and drug interactions

c. ability to monitor with standard laboratory equipment

d. availability of numerous reversal agents

Chapter 15

Urinary System Drugs

Key Terms and Concepts

Alpha-blockers
Antiandrogens
Antispasmodics
Benign prostatic hyperplasia (BPH)
Bladder antispasmodics
Calculus
Cholinergic
Diuretics
Gout
Hyperkalemia
Hypertonic
Hypokalemia
Hypotonic
Osmotic agents
Overactive bladder (OAB)
Uricosuric agents
Urinary analgesic

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe the four types of diuretics in terms of uses, side effects, precautions and contraindications, and interactions and give examples of each type.
2. Identify and describe medications given for acute and chronic gout; include side effects, precautions and contraindications, and drug interactions.
3. Explain the role of certain antispasmodics used to reduce contractions of the urinary bladder.
4. Identify the actions, uses, side effects, and precautions and contraindications for urinary analgesics to treat pain and cholinergic agents to stimulate bladder contraction.
5. Describe the three different treatments for benign prostatic hyperplasia (BPH).

Diuretics

The most commonly used drugs influencing the function of the urinary tract are the **diuretics**, which increase urine excretion. Their main indication is to reduce the circulating fluid volume to help treat edema and hypertension. Diuretics are divided into five categories according to their action: thiazides, loop diuretics, potassium-sparing diuretics, osmotic agents, and carbonic anhydrase inhibitors. Carbonic anhydrase inhibitors such as acetazolamide (Diamox), which are used to lower intraocular pressure.

Thiazides and Related Diuretics

Thiazides are the most frequently used type of diuretic, increasing excretion of water, sodium, chloride, and potassium. An example is hydrochlorothiazide.

Uses of thiazides include treatment of:

- Edema from many causes (e.g., heart failure and cirrhosis), although loop diuretics are more commonly used
- Hypertension, either alone or combined with drugs from other classes (blood pressure is lowered by reducing peripheral vascular resistance as well as by decreasing fluid retention)
- Prophylaxis of **calculus** (stone) formation in those with hypercalciuria (excess calcium in the urine)

Side effects of thiazides may include:

- ❗ **Hypokalemia** (potassium deficiency), which may lead to cardiac arrhythmias; hyponatremia (low serum sodium level); hypercalcemia (abnormally high blood calcium level)
- ❗ Muscle weakness or spasm
- ❗ Postural hypotension, vertigo, and headache
- Skin conditions (e.g., rash and photosensitivity)

Cautions or contraindications with thiazides apply to:

- Diabetes (may cause hyperglycemia and glycosuria)
- History of gout (increased uric acid level)
- Severe renal disease
- Impaired liver function
- Prolonged use (periodic serum electrolyte checks are indicated, and potassium supplements may be necessary to prevent hypokalemia)
- Older adults because of greater sensitivity to thiazides (may cause low sodium level)
- Patients with sulfonamide hypersensitivity

Interactions of thiazides may occur with:

- Nonsteroidal anti-inflammatory agents (risk of renal insufficiency and reduced blood pressure control)
- Corticosteroids (increase potassium loss)
- Lithium (causes lithium intoxication)
- Hypotensive agents (potentiate blood pressure decrease)
- Digoxin (increased potential for digoxin toxicity)
- Probenecid (blocks uric acid retention)
- Antidiabetic agents (loss of diabetic control)

Patient Education

Patients being treated with thiazides should be instructed regarding:

- Diet including potassium-rich foods (e.g., citrus fruits and bananas) or potassium supplements (check with the physician first)
- A low-sodium diet prescribed by the physician if the diuretic is prescribed for hypertension
- Administration with food (to reduce gastric irritation)
- Administration in the morning to prevent disruption of sleep from frequent urination
- Rising slowly from a reclining position to counteract postural hypotension
- Limiting alcohol consumption
- Necessity for regular blood tests with chronic use to monitor electrolyte levels

Loop Diuretics

These diuretics act directly on the loop of Henle in the kidney to inhibit sodium and chloride reabsorption, which in turn inhibits water reabsorption back into the bloodstream, leading to increased urine formation. Potent diuretics such as furosemide (Lasix), bumetanide (Bumex), and torsemide (Demadex) are not thiazides but act in a similar way to increase the excretion of water, sodium, chloride, and potassium. Their action is more rapid and effective than that of thiazides, with a greater *diuresis* (although they do not lower blood pressure as well as the thiazides).

Uses of loop diuretics include treatment of:

- Edema associated with impaired renal function, heart failure, or hepatic disease
- Pulmonary edema
- Ascites caused by malignancy or cirrhosis
- Hypertension (if thiazides are ineffective, loop diuretics are sometimes combined with other antihypertensives, especially in patients with kidney disease)

Side effects of loop diuretics may include:

- ❗ Fluid and electrolyte imbalance with dehydration, circulatory collapse, and chest pain
- ❗ Hypokalemia with weakness (potassium supplements may be indicated, especially for cardiac patients to prevent arrhythmias); hypocalcemia (abnormally low blood calcium level)
- ❗ Hypotension (close blood pressure checks are required)
- Tinnitus, hearing impairment, and blurred vision
- Rash, urticaria, pruritus, and photosensitivity
- Headache, muscle cramps, mental confusion, and dizziness

Cautions or contraindications with loop diuretics apply to:

- Cirrhosis and other liver disease (careful monitoring is required)
- Kidney impairment
- Alkalosis and dehydration
- Patients on digoxin (cardiac arrhythmias are possible unless potassium is supplemented)

Those allergic to sulfonamides
Diabetes (may cause hyperglycemia and glycosuria)
History of gout (increased uric acid level)
Pregnancy and lactation
Patients under 18 years of age (bumetanide and torsemide)

Interactions of loop diuretics are similar to those of thiazides:

Corticosteroids (potentiate potassium loss)
Lithium (toxicity risk is increased)
Hypotensive agents (potentiation of effects)
Digoxin (increased potential for digoxin toxicity and arrhythmias)

Additional interactions of loop diuretics may include:

Aminoglycosides increase the chance of deafness.
Indomethacin decreases the diuretic effect.
Salicylates with furosemide increase the chance of salicylate toxicity.
Anticonvulsants (e.g., phenytoin) reduce the diuretic effect of furosemide.

Patient Education

Patients being treated with loop diuretics should be instructed regarding the same information as patients taking thiazides.

Potassium-Sparing Diuretics

Potassium-sparing diuretics such as spironolactone (Aldactone), eplerenone (Inspra), and triamterene (Dyrenium) are primarily used under conditions in which potassium depletion can be dangerous or undesirable. Potassium-sparing diuretics may also counteract the increased glucose and uric acid levels associated with thiazide diuretic therapy. Spironolactone is the diuretic of choice in patients with cirrhosis. It has also been shown to reduce deaths in patients with severe heart failure.

Potassium-sparing (saving) diuretics are seldom used alone but are usually combined with thiazide diuretics to increase the diuretic and hypotensive effects and to reduce the danger of **hyperkalemia** (excessive potassium retention). When combination products (e.g., Aldactazide or Dyazide) are given, supplemental potassium is usually *not* indicated, but this varies with individual circumstances and other medications taken concomitantly. *Periodic serum electrolyte checks are indicated.*

Side effects of potassium-sparing diuretics are usually mild and respond to withdrawal of the drug, but may include:

! *Hyperkalemia* (especially with potassium supplements), which may lead to *cardiac arrhythmias*

Dehydration or weakness

- GI symptoms, including nausea, vomiting, and diarrhea
- ❗ Fatigue, lethargy, and profound weight loss
- ❗ Hypotension
- ❗ Gynecomastia (enlargement of breast tissue in males) with spironolactone

Caution with potassium-sparing diuretics is indicated in patients with:

- Renal insufficiency
- Cirrhosis and other liver disease
- Pregnancy and lactation

Interactions may occur to cause hyperkalemia between potassium-sparing diuretics and:

- Potassium supplements, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), salicylates, and nonsteroidal anti-inflammatory drugs (NSAIDs)

Osmotic Agents

Osmotic agents (e.g., mannitol) are most frequently used to reduce intracranial or intraocular pressure. These agents are used mostly in emergency situations that involve cranial or spinal trauma and are used to reduce the risk of nervous system damage from swelling.

Side effects of osmotic agents can include:

- ❗ Fluid and electrolyte imbalance
- ❗ CNS symptoms, including headache, vertigo, and mental confusion
- ❗ GI symptoms, including nausea and vomiting
- ❗ Tachycardia, hypertension, and hypotension
- ❗ Allergic reactions
- ❗ Severe pulmonary edema

Extreme caution is indicated, and kidney and cardiovascular function should be evaluated before administration of osmotic agents to anyone with:

- Kidney failure
- Heart failure
- Severe pulmonary edema
- Pregnancy and lactation

Patient Education

Patients being treated with potassium-sparing diuretics should be instructed regarding:

- Avoiding potassium-rich foods and salt substitutes
- Reporting signs of excessive dehydration (e.g., dry mouth, drowsiness, lethargy, and fever)
- Reporting GI symptoms (e.g., nausea, vomiting, and diarrhea)
- Reporting persistent headache and mental confusion
- Reporting irregular heartbeat
- Monitoring weight and reporting sudden, excessive weight loss
- Rising slowly from a reclining position
- Taking medications after meals

Patient Education

Patients being treated with osmotic agents should be instructed regarding side effects to be reported to the physician immediately. The patient should be reassured that osmotic agents are always given under close medical supervision, and serum electrolyte levels will be monitored frequently by blood tests to detect adverse reactions.

Table 15-1 provides a summary of drugs for diuresis.

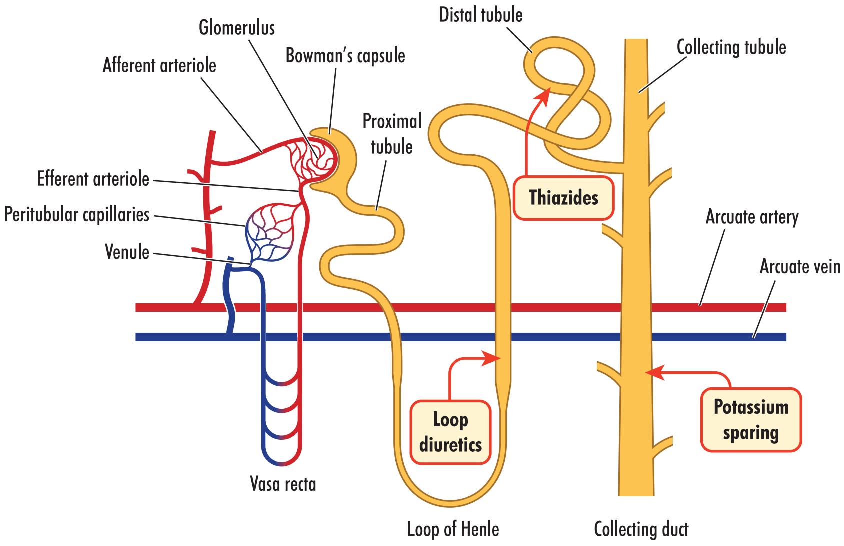
Table 15-1 Drugs for Diuresis

Generic Name	Trade Name	Dosage (Varies with Condition)[a]
Thiazide and Related Diuretics (Representative List—Many Others)		
Hydrochlorothiazide	Microzide/HCTZ	12.5–100 mg daily
metolazone	Zaroxolyn	2.5–20 mg daily
indapamide	Lozol	2.5–2 mg daily
Loop Diuretics		
furosemide	Lasix	20–80 mg daily or bid[c], PO, IM, or IV
bumetanide	Bumex[b]	0.5–2 mg daily or bid[c], PO, IM, or IV
torsemide	Demadex	5–20 mg daily or bid[c], PO; slow IV dosage not to exceed 200 mg *do not give IM*
Potassium-Sparing Diuretics		
spironolactone	Aldactone	25–100 mg daily
triamterene	Dyrenium	50–100 mg bid pc
eplerenone	Inspra	25–50 mg daily
Combination Potassium-Sparing and Thiazide Diuretics		
spironolactone and hydrochlorothiazide	Aldactazide	25–50 mg daily (each component)
triamterene and hydrochlorothiazide	Dyazide, Maxzide	37.5 mg/25 mg, 50 mg/25 mg, 75 mg/50 mg 1 cap or tab daily
Osmotic Agents		
mannitol	Osmitrol	Parenteral only; dose varies with condition

[a] Dose may be higher for edema and heart failure.
[b] This brand name is no longer marketed, but the name is still commonly used.
[c] bid dosing is most often associated with the treatment of heart failure. Patients should be instructed to take the second dose in the middle of the day to avoid nighttime urination.

Learning Hint

Trying to understand how diuretics work to increase fluid (water) excretion can be confusing. The easiest way to think about this is to recognize that when two solutions are separated by a permeable barrier, water will cross the permeable barrier in the direction of the higher salt (electrolyte) concentration. When a solution has a higher salt concentration relative to another solution, it is termed **hypertonic**. The solution with the lower concentration of salt is termed **hypotonic**, and water flows away from this solution. This is how the urinary system functions. Remembering the phrase "water follows salt," may help you better visualize how diuretics function. Through various mechanisms and in various parts of the renal system, all diuretics act to increase the amount of salt in the urine, which increases its hypertonicity. This pulls more water into the urine (or inhibits it from being reabsorbed), which means more water will be excreted. While all electrolytes can affect hyper- and hypotonicity, sodium is the most impactful. Figure 15-1 illustrates how each diuretic class works in the urinary system.


Glomerulus
Distal tubule
Afferent arteriole
Bowman's capsule
Collecting tubule
Proximal tubule
Efferent arteriole
Peritubular capillaries
Thiazides
Arcuate artery
Venule
Arcuate vein
Loop diuretics
Potassium sparing
Vasa recta
Loop of Henle
Collecting duct

Blamb/Shutterstock.com.

Figure 15-1 How and where diuretics work.

Potassium Sparing

Mechanism of action: Potassium-sparing diuretics bind to sodium-potassium ATPase transporters, which interferes with sodium and potassium exchange in multiple places in the kidney, but primarily in the collecting duct. This causes an increase in sodium excretion while decreasing potassium excretion.
Example: spironolactone

Loop Diuretics

Mechanism of action: Loop diuretics bind to chloride channel receptors in the ascending limb of the loop of Henle, inhibiting the reabsorption of sodium and chloride. This inhibits water reabsorption by the collecting tubules by increasing hypertonicity.
Example: furosemide

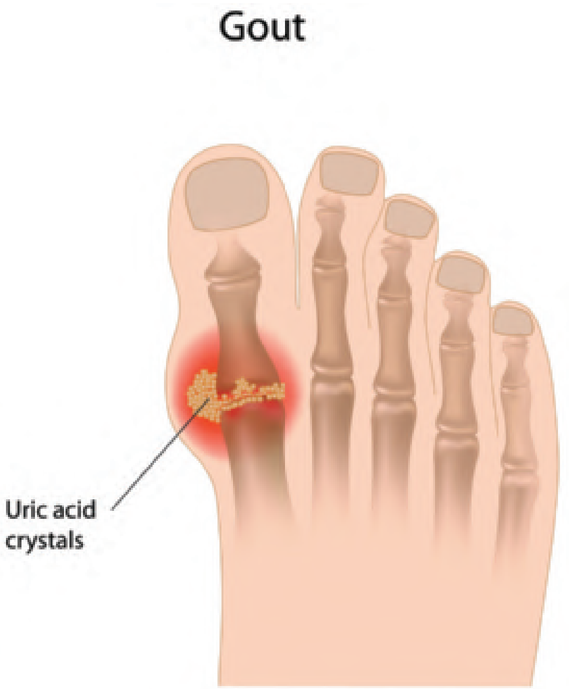
Thiazides

Mechanism of action: Thiazides increase salt (electrolyte) and water excretion by inhibiting mechanisms for sodium and chloride transport in the distal convoluted tubule. This inhibits water reabsorption by the collecting tubules by increasing hypertonicity.
Example: hydrochlorothiazide

Medications for Gout

Gout is a metabolic disorder characterized by the accumulation of uric acid crystals in various joints (especially the big toe, ankle, knee, and elbow), tissues, and sometimes the kidneys, with resultant inflammation and pain (Figure 15-2). The management of gout includes treating acute attacks, uric acid-lowering therapy, and preventing the recurrence of acute attacks.

Acute gout is characterized by the sudden onset of pain, redness, warmth, and swelling in the affected joints. It occurs most commonly at night and in patients who are not well hydrated. Patients who are affected by gout can take nonpharmacological measures to help control their condition. Staying hydrated and avoiding or limiting fruit juices, seafood, red meats, and foods that are high in sugar and salt are dietary measures that help reduce the risk of acute gouty attacks. Smoking cessation and limiting alcohol consumption will also help.



Alila Medical Media/Shutterstock.com.

Figure 15-2 Gout of the big toe due to uric acid formation.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs), Corticosteroids, and Colchicine

NSAIDs such as naproxen, indomethacin, and ibuprofen, when started soon after the onset of symptoms, work quickly to relieve pain. NSAIDs should be used cautiously in patients with kidney disease, heart disease, or risk factors for GI bleeding. Corticosteroids such as prednisone are useful in the treatment of acute gout in patients who cannot tolerate NSAIDs.

Colchicine is not an analgesic and does not affect uric acid clearance. It is used to relieve inflammation in acute gouty arthritis (must be given within 24 h of the onset of symptoms for maximum effectiveness) and in the chronic management of gout. Colchicine can also be used prophylactically at low doses to prevent recurrent attacks.

Side effects of colchicine limit its use and can include:

Rash, alopecia

! GI upset, nausea, vomiting, and diarrhea (about 80% of patients cannot tolerate the frequent GI side effects)

Blood disorders and bone marrow suppression

Patient Education

Patients being treated with colchicine should be instructed regarding:

Large fluid intake to facilitate excretion of uric acid crystals.

Avoiding alcohol (increases the risk of adverse GI effects and increases serum urate [salt of uric acid] concentrations)

Medications used to treat gout chronically include the uricosuric agents, the xanthine oxidase inhibitors, and PEGylated uric acid specific enzymes. All these medications lower uric acid levels in different ways.

Uricosuric Agents

Uricosuric agents, such as probenecid, act on the kidneys by blocking reabsorption and thereby promoting urinary excretion of uric acid. This type of drug is used in the treatment of chronic cases of gout and frequent disabling attacks of gouty arthritis. However, the uricosuric agents have no analgesic or anti-inflammatory activity and are therefore not effective in the treatment of acute gout. During acute attacks of gout, the probenecid dosage is supplemented with colchicine, which has an anti-inflammatory action.

Probenecid is sometimes given with penicillin to potentiate the level of the antibiotic in the blood, for example, with amoxicillin for some gonococcal infections. Probenecid is also given with cefoxitin to treat acute pelvic inflammatory disease.

Side effects of probenecid are rare but may include:

Headache
Nausea and vomiting
! Kidney stones and renal colic if a large volume of fluids is not maintained
Hypersensitivity reactions, rash, hypotension, and anaphylaxis are rare

Cautions or contraindications for probenecid apply to patients with:

History of uric acid kidney stones
History of peptic ulcer
Renal impairment
Hematologic disease

Interactions may occur with:

Penicillins and cephalosporins, potentiating therapeutic effect of antibiotics
Oral hypoglycemics, which could cause hypoglycemia through potentiation
Salicylates, which antagonize uricosuric action
NSAIDs (probenecid decreases renal clearance)

Patient Education

Patients being treated with uricosuric agents should be instructed regarding:

Drinking large amounts of fluid
Avoiding taking large doses of aspirin products (aspirin doses of 325 mg per day or less are okay)
Taking other medications at the same time only with the physician's order
Taking medications with food
Reporting rash immediately

Xanthine Oxidase Inhibitors

Allopurinol (Zyloprim) is another medication used to treat chronic gout. This class of drugs also results in decreased serum and urinary levels of uric acid. It has no analgesic or anti-inflammatory activity and therefore is not effective in the treatment of acute gout. If xanthine oxidase inhibitor therapy is initiated during an acute gout attack, it can make the attack worse.

Allopurinol is also used for the prevention of renal calculi in patients with a history of frequent stone formation and prevention of acute hyperuricemia during radiation of certain tumors or antineoplastic therapy.

Febuxostat (Uloric) is the first new oral agent approved for gout since the early 1960s. It is more potent and has a lower risk of hypersensitivity reactions compared to allopurinol. Febuxostat may have a higher risk of cardiovascular adverse events.

Side effects of allopurinol can include:

Rash
❗ Allergic reactions; also fever, chills, nausea, vomiting, diarrhea, drowsiness, and vertigo
Severe hypersensitivity reactions are rare, but increase in older patients with renal impairment who receive allopurinol and thiazide diuretics in combination

Cautions or contraindications with allopurinol apply to:

Impaired renal function
History of hypersensitivity reactions
Liver disease
Pregnancy and lactation

Interactions of allopurinol may occur with:

Antineoplastic drugs (potentiate side effects—azathioprine, mercaptopurine)
Alcohol and diuretics (increase serum urate concentrations)

PEGylated Uric Acid Specific Enzymes

Pegloticase (Krystexxa) is a newer class of gout treatment that lowers uric acid by causing the oxidation of uric acid to a non-gout causing compound called allantoin, which is easily excreted through the renal system. It is reserved for patients who are resistant to other therapies and is given via IV infusion every 2 weeks.

Side effects of pegloticase can include:

❗ Infusion reactions
❗ Formation of anti-pegloticase antibodies
Rebound gout flares

Cautions or contraindications with pegloticase apply to:

❗ G6PD deficiency; patients at higher risk for G6PD deficiency (African or Mediterranean ancestry) should be screened before starting pegloticase
Pregnancy

Patient Education

Patients being treated with allopurinol and febuxostat should be instructed regarding:

- Drinking large quantities of fluid
- Taking medication after meals
- Stopping medication and reporting rash to the physician immediately
- Avoiding alcohol, which increases uric acid
- Avoiding purine-rich foods (liver, kidneys, shellfish, and red meat)
- Avoiding other medications unless prescribed by the physician

Monoclonal Antibodies Used for Gout

Canakinumab (Ilaris) is a monoclonal antibody that helps relieve symptoms of acute gout flares. It is the first and only biologic approved for the treatment of gout flares. It is used in patients who cannot be treated with NSAIDs, colchicine, or repeated courses of corticosteroids. It is administered as a single subcutaneous injection at the onset of a gout flare-up.

Side effects of pegloticase can include:

- ❗ Injection site irritation
- ❗ Nasopharyngitis
- Diarrhea

Table 15-2 provides a summary of drugs for gout.

Table 15-2 Antigout Medications

Generic Name	Trade Name	Dosage
colchicine	Colcrys	PO 0.6–1.2 mg daily in div. doses
Uricosuric Agents		
probenecid		250–500 mg bid
probenecid w/colchicine		1 tab (500 mg/0.5 mg) bid
Xanthine Oxidase Inhibitors		
allopurinol	Zyloprim	100–600 mg daily
febuxostat	Uloric	40–80 mg daily
PEGylated Uric Acid Specific Enzymes		
pegloticase	Krystexxa	8 mg/mL IV infused over 2 weeks
Monoclonal Antibodies		
canakinumab	Ilaris	150 mg SQ at onset of gout flare (must wait 12 weeks before using again)

Bladder Antispasmodics

Overactive bladder (OAB) is a condition characterized by two urinary symptoms: *frequency* and *urgency*. Frequency is defined as having to urinate more than 8 times in 24 h; urgency means the sudden need to urinate.

Antispasmodics, which are **anticholinergic** in action (blocking parasympathetic nerve impulses), are used to increase the capacity and decrease the urgency of the urinary bladder. Antispasmodics, such as tolterodine (Detrol) and oxybutynin (Ditropan), are used to decrease bladder tone and suppress bladder contractions in patients with neurogenic bladder, resulting in decreased incontinence.

These drugs are used for the relief of symptoms such as urgency, frequency, nocturia, and incontinence. They have similar adverse side effects, especially in older adults.

Extended-release formulations (Ditropan XL, Detrol LA), patches (Oxytrol) and newer agents (Enablex, VESIcare) are less effective than or equally as effective as oxybutynin IR (immediate release) but may cause fewer anticholinergic adverse effects. Recently the FDA approved an OTC patch called *Oxytrol for Women* (18 years or older); the Oxytrol patch remains prescription-only for men.

Side effects of the **bladder antispasmodics** are due to the ***anticholinergic*** actions of these drugs and can include:

- ❗ Drying of all secretions
- ❗ Urinary retention and constipation (dose too high)
- ❗ Blurred vision (due to dry eye)
- ❗ Mental confusion (especially with older adults)
- ❗ Tachycardia, palpitations

Cautions or contraindications with bladder antispasmodics apply for:

Hepatic or renal disease and obstructive uropathy
Bladder or GI obstruction, or ulcerative colitis
Cardiovascular disease
Prostatic hyperplasia
Children—contraindicated for those under 6 years of age; Ditropan XL is used effectively in children 6 years of age and older
Pregnancy or lactation
Narrow-angle glaucoma

Interactions with bladder antispasmodics may include:

Other anticholinergic agents (can potentiate effects with possible toxicity)
Potassium salts (risk of GI irritation)

Mirabegron (Myrbetriq) and vibegron (Gemtesa) are the newest bladder antispasmodics. They stimulate beta$_3$ receptors in the bladder to increase bladder capacity. It provides an alternative for patients who cannot tolerate the side effects of the anticholinergic antispasmodics. Common adverse effects of mirabegron and vibegron include nausea, constipation, diarrhea, headache, dizziness, hypertension, and sinus tachycardia.

Learning Hint

As mentioned, anticholinergics cause the drying of all bodily secretions. This can lead to various side effects, with the most common being dry eyes and dry mouth. Although dose adjustment (decrease) can be an effective way to manage side effects, many times it is difficult to find a balance between adequate effectiveness and the extent of adverse effects of anticholinergics. Therefore, it is often a better option to treat these side effects rather than eliminate them. OTC ophthalmic lubricating drops and artificial tears are options for treating dry eye, with prescription drops reserved for severe cases. Dry mouth can be managed by OTC lozenges and oral rinses that promote natural saliva production. As with any side effects, properly educating patients about those that may occur and how to manage them is an important factor in patient compliance.

Patient Education

Patients being treated with bladder antispasmodics should be instructed regarding:

- Possible interactions with other drugs
- Reporting side effects that are troublesome for possible dosage adjustment
- Reporting effectiveness—inform patients that it may take several months to notice effects
- Using caution while driving or operating machinery
- Avoiding alcohol or other sedatives that potentiate drowsiness
- Seeking the advice of a health care professional before using over-the-counter *Oxytrol for Women*, to understand all of the FDA-required safe conditions for use
- Not crushing or chewing extended-release formulations (Enablex, Toviaz); not cutting or trimming patches (Oxytrol)
- Bladder retraining, toileting programs, and pelvic-floor exercises (Kegels), which may also be prescribed to improve bladder function

Cholinergics

Bethanechol (Urecholine) is a **cholinergic** drug, stimulating parasympathetic nerves to bring about contraction of the urinary bladder in cases of nonobstructive urinary retention, usually postoperatively or postpartum. It has been called the pharmacological catheterization.

Side effects of bethanechol are cholinergic in action and usually dose related, and can include:

- ! GI cramping, diarrhea, nausea, and vomiting
- ! Sweating and salivation
- ! Headache and bronchial constriction
- ! Slow heartbeat or reflex tachycardia and orthostatic hypotension
- ! Urinary urgency

Cautions or contraindications of bethanechol include:

- Obstruction of the GI or urinary tract
- Hyperthyroidism
- Peptic ulcer and irritable bowel syndrome
- Asthma

Cardiovascular disease—bradycardia
Parkinsonism and seizure disorder
Pregnancy and lactation

Interactions with bethanechol may occur with:

Other cholinergic or anticholinesterase agents (e.g., neostigmine) administered concomitantly (can potentiate effects, with increased possibility of toxicity)
Quinidine or procainamide (antagonize cholinergic effect)
Atropine (antagonizes cholinergic effect—antidote in cases of cholinergic toxicity)

Urinary Analgesics

Phenazopyridine (AZO Standard) is an oral **urinary analgesic** or local anesthetic for urinary tract mucosa. It is used for a short time to relieve burning, pain, discomfort, and urgency associated with cystitis (bladder inflammation). It should not be taken for more than 2 days when used with an antibacterial agent.

Clinical Application

Urinary Tract Infections

Urinary tract infections (UTIs) are characterized by symptoms that include increased frequency of urination or sudden urge to urinate, burning while urinating, cloudy or strong-smelling urine, and possible pain in the lower abdominal area (Figure 15-3). UTIs are most common in women, and the frequency of occurrence increases with age. In older adult patients, UTIs can often present with psychological symptoms that include confusion and delirium. Some common antibiotics that are used for UTI treatment are Bactrim, Cipro, and Macrobid for a period of 7–14 days. Patients who have a history of UTIs should be educated to use proper hygiene and stay hydrated. As a health care professional, it is important to educate patients that although UTIs can resolve without treatment, it is important to seek treatment to avoid complications such as a kidney infection or damage to the urinary system.

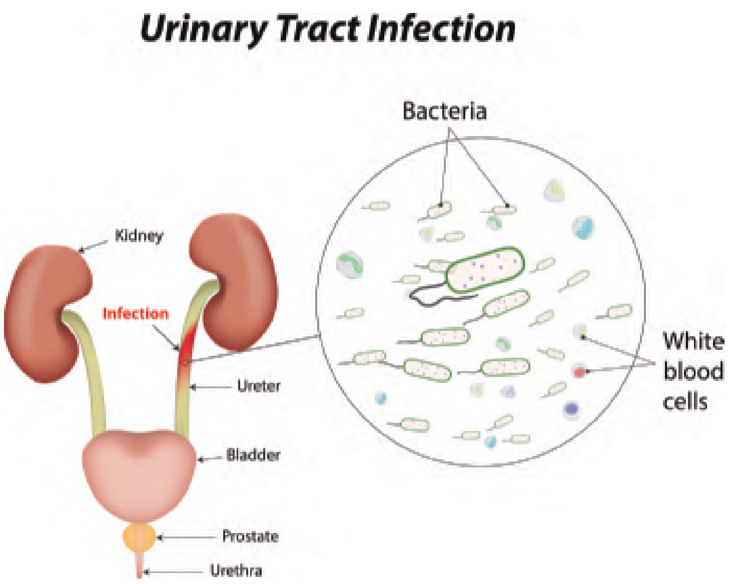


Figure 15-3 If left untreated, an uncomplicated UTI can travel up the ureter into the kidney and cause a more complicated infection called pyelonephritis.

joshya/Shutterstock.com.

Phenazopyridine is used *only for symptomatic* relief while waiting to see a physician and is not a substitute for the treatment of causative conditions. For treatment of urinary tract infections, anti-infective medication is required.

Side effects of phenazopyridine are rare for the most part but can include:

Headache or vertigo

GI disturbances

❗ Discoloration of bodily fluids, including orange-red urine (common), which may stain fabric; causes discoloration of contact lenses

Cautions or contraindications for urinary analgesics include:

Impaired kidney function, especially in older adults

Phenazopyridine may interfere with blood glucose measurements and urine ketone and protein kidney tests

Table 15-3 provides a summary of drugs for bladder incontinence.

Table 15-3 Bladder Antispasmodics

Generic Name	Trade Name	Dosage
Anticholinergics		
tolterodine	Detrol	1–2 mg bid
	Detrol LA	2–4 mg daily
oxybutynin	Ditropan[a] Ditropan XL	2.5–5 mg two to four times per day
	Oxytrol patch (Rx)	5–30 mg daily
	Oxytrol for Women (OTC)	3.9 mg per day patch twice weekly
darifenacin	Enablex	7.5–15 mg daily
fesoterodine	Toviaz	4–8 mg daily
solifenacin	VESIcare	5–10 mg daily
Beta$_3$ Agonists		
mirabegron	Myrbetriq	25–50 mg daily
vibegron	Gemtesa	75 mg daily
Cholinergic[b]		
bethanechol	Urecholine	10–50 mg three to four times per day
Analgesic		
phenazopyridine	(Pyridium)[a] (Rx)	100–200 mg tid pc for 48 h only
	AZO Standard (OTC)	Dose varies depending on age range

[a] This brand name is no longer marketed, but the name is still commonly used.

[b] For bladder contraction.

Patient Education

Patients being treated with phenazopyridine for urinary tract distress should be instructed regarding color change of urine to orange-red, which may stain fabric, and tears that may stain contact lenses.

Phenazopyridine is only temporarily effective against discomfort in the lower urinary tract and is not effective against infection. The cause of the discomfort must be determined and appropriate therapy, such as surgery or anti-infective medication, may be necessary to correct the condition.

Treatment of Benign Prostatic Hyperplasia

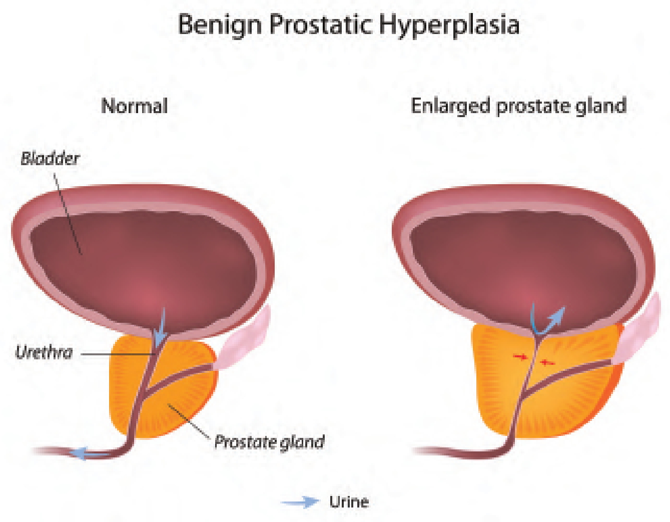
Benign prostatic hyperplasia (BPH) is the most common benign tumor in males. BPH involves *hyperplasia* (an increase in the number of cells) leading to prostate enlargement, which interferes with urinary flow (Figure 15-4).

Drugs used to treat the symptoms of BPH include those that slow prostate growth (antiandrogens) and those that relax the bladder smooth muscle to make it easier for urine to flow from the bladder through the urethra (alpha-blockers).

Antiandrogens (5-alpha reductase inhibitors)

Finasteride (Proscar) and dutasteride (Avodart) work by suppressing prostate growth and associated urinary obstruction and manifestations, for example, urgency, nocturia, and urinary hesitancy. Proscar 5 mg, or Avodart 0.5 mg, is administered daily for a minimum of 6–12 months. This therapy appears to be suppressive rather than curative, and return of the hyperplasia is likely if the drug is withdrawn.

Side effects of **antiandrogens** include impotence, decreased libido, decreased ejaculate, and gynecomastia (including breast tenderness and enlargement). Side effects diminish after the first year of treatment.



Alila Medical Media/Shutterstock.com

Figure 15-4 Benign prostatic hyperplasia (BPH).

Cautions: Patients should be screened first for cancer, infection, or other urinary dysfunctions. Antiandrogens can affect a blood test called PSA, used for the screening of prostate cancer (serum PSA concentrations may decrease even in the presence of prostate cancer). Liver function abnormalities may be exacerbated. Crushed tablets and soft gelatin capsules should *not be handled by pregnant women* (they can cause fetal damage).

Antiandrogens have not been associated with clinically important *drug interactions.*

Saw palmetto is a commonly used supplement for BPH, which might moderately reduce some BPH symptoms. The effects of co-use are not known at this time.

Alpha-Blockers

Tamsulosin (Flomax) blocks alpha$_1$ receptors found in smooth muscle in the bladder neck and prostate, causing them to relax. Consequently, the urine flow rate is improved and the symptoms of BPH are decreased. Alpha-blockers are considered to be the first-line therapy for the treatment of BPH. Other examples of **alpha-blockers** are doxazosin (Cardura) and terazosin (Hytrin), which are used in the treatment of hypertension, as well as for BPH.

Side effects of alpha-blockers are infrequent but can include:

❗ Dizziness, headache, and nasal congestion
❗ Orthostatic hypotension
Palpitations (not Flomax)
Ejaculation dysfunction, decreased libido, and impotence

Cautions: Patients with a history of serious or life-threatening sulfonamide allergy (with Flomax):

Notify ophthalmologist of current or previous treatment with alpha-blockers—may be at risk for intraoperative floppy iris syndrome during cataract surgery.

Interactions may occur with:

Calcium channel blockers
Other antihypertensive agents (additive hypotensive effects)

Combination therapy with an antiandrogen (Proscar) and an alpha-blocker (Cardura) in patients with large prostates may significantly reduce the overall clinical progression of BPH and may reduce the need for invasive therapy compared to either agent alone (more data is needed, however).

Phosphodiesterase (PDE) Inhibitor

Tadalafil (Cialis), a PDE inhibitor approved for the treatment of erectile dysfunction, was recently approved to treat the signs and symptoms of BPH when taken daily.

Caution: It is important to read the specific instructions on the product label to reduce the risk of hypotension and fainting.

Table 15-4 provides a summary of drugs for benign prostatic hyperplasia.

Table 15-4 Agents for BPH

Generic Name	Trade Name	Dosage
Antiandrogens (5-alpha reductase inhibitors)		
finasteride	Proscar	5 mg daily
dutasteride	Avodart	0.5 mg daily
Alpha-Blockers		
alfuzosin	Uroxatral	10 mg daily with a meal
doxazosin	Cardura	1–8 mg at bedtime
silodosin	Rapaflo	4–8 daily with a meal
tamsulosin	Flomax	0.4–0.8 mg once daily 30 min after same meal or HS
terazosin	Hytrin[a]	1–10 mg at bedtime
Phosphodiesterase Inhibitor		
tadalafil	Cialis	5 mg daily
Combination Phosphodiesterase Inhibitor/Antiandrogen (5-alpha reductase inhibitor)		
finasteride/tadalafil	Entadfi	1 capsule (5 mg/5 mg) daily

[a] This brand name is no longer marketed, but the name is still commonly used.

Case Study A

Urinary System Drugs

A 68-year-old patient is admitted to the hospital with shortness of breath, swollen ankles, and fatigue. The patient's diagnosis is pulmonary edema.

1. The patient's physician prescribes a loop diuretic, which acts directly on what part of the kidney?
a. nephrons
b. Bowman's capsule
c. renal pelvis
d. loop of Henle

2. The primary action of loop diuretics is to:
a. increase the excretion of water, sodium, chloride, and potassium
b. inhibit H_2O reabsorption back into the bloodstream
c. reduce peripheral vascular resistance
d. decrease fluid retention by promoting the excretion of uric acid

3. A potential side effect of a loop diuretic is:
a. hypokalemia
b. hypertension
c. hyperkalemia
d. renal colic

4. The nurse is preparing the patient for discharge and instructs them on how to take their daily medication. One important point to include is to:

a. get 4 h of sunshine a day
b. take medications at bedtime
c. avoid eating bananas
d. rise slowly from a reclining position

5. The nurse also makes sure that they review potential interactions with other medications and advise the patient to avoid:

a. NSAIDs
b. diphenhydramine
c. digoxin
d. anticonvulsants

Case Study B

Urinary System Drugs

A 30-year-old patient is visiting their OB/GYN for their 6-week postpartum checkup. The patient complains of burning, pain, and discomfort upon urination. Their physician prescribes a urinary analgesic to help relieve these symptoms.

1. The physician explains to the patient that urinary analgesics are given for a short time to alleviate symptoms associated with:

a. incontinence
b. nocturia
c. cystitis
d. prostatic hyperplasia

2. After giving the patient the prescription, the physician explains that the medication phenazopyridine can change the color of the patient's urine. What color might their urine be while on this medication?

a. deep yellow
b. pink-tinged
c. pale yellow
d. orange-red

3. The physician also educates the patient on possible side effects of phenazopyridine, which include:

a. vertigo
b. fatigue
c. palpitations
d. nasal congestion

4. Prior to prescribing the medication, the physician reviews the patient's chart to make sure they do not have a cautionary condition. Patients with what condition would need to avoid phenazopyridine?

a. cardiovascular disease
b. BPH
c. impaired kidney function
d. asthma

5. The physician also prescribes an antibiotic to be taken along with the phenazopyridine. Because of this, the physician explains to the patient that they should only take phenazopyridine for how many days?

a. 2
b. 4
c. 6
d. 8

Chapter Review Quiz

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication	Condition
1. ______ Proscar	**a.** Congestive heart failure
2. ______ probenecid	**b.** Gout
3. ______ Hydrochlorothiazide	**c.** Benign prostatic hyperplasia (BPH)
4. ______ Ditropan XL	**d.** Incontinence
5. ______ Allopurinol	**e.** Edema
6. ______ Lasix	
7. ______ Cardura	
8. ______ Detrol	
9. ______ Demadex	
10. ______ Microzid	

Choose the correct answer.

11. Which medication is used prophylactically at low doses to prevent recurrent attacks of gout?

a. Naprosyn
b. ibuprofen
c. indomethacin
d. colchicine

12. What type of intake is suggested for a patient on probenecid to prevent kidney stones and renal colic?

a. low sodium
b. large volume of fluids
c. low potassium
d. acidic fluids

13. Which instruction should be given to a patient taking allopurinol?

a. Eat purine-rich foods.
b. Avoid alcohol.
c. Take medication with meals.
d. Expect a slight rash.

14. In treating BPH, a patient taking Flomax might experience which side effect?

a. hypertension
b. dizziness
c. palpitations
d. hyperglycemia

15. What is a symptom or condition that is characterized by having to urinate more than 8 times in 24 h?

a. nocturia
b. frequency
c. urgency
d. incontinence

16. Which of the following is the most uncommon medication used to treat a UTI?

a. Macrobid
b. phenazopyridine
c. Bactrim DS
d. oxybutynin

17. In which area of the renal system do loop diuretics primarily function?

a. loop of Henle
b. collecting duct
c. distal tubule
d. proximal tubule

18. Which diuretic would be considered potassium sparing?

a. hydrochlorothiazide
b. furosemide
c. spironolactone
d. bumetanide

19. Using the renal system as an example, what is true regarding the flow of water across a permeable barrier?

a. Water will flow in the direction that contains less sodium.
b. Water will flow in the direction that contains a hypotonic solution.
c. Water flow is not affected by sodium concentration.
d. Water will flow in the direction that contains a hypertonic solution.

20. Patients with gout can be initiated on allopurinol therapy during an active gout attack.

a. True
b. False

Chapter 16

Gastrointestinal Drugs

Key Terms and Concepts

Antacids

Antidiarrheal

Antiemetics

Antiflatulents

Antispasmodics

Antiulcer

Chemotherapy-induced nausea and vomiting (CINV)

Emesis

Gastroesophageal reflux disease (GERD)

Histamine$_2$ blockers

Inflammatory bowel disease (IBD)

Laxatives

Postoperative nausea and vomiting (PONV)

Probiotics

Proton pump inhibitor (PPI)

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe uses, side effects, precautions and contraindications, and interactions of antacids, antiulcer agents and agents for gastroesophageal reflux disease (GERD), agents for irritable bowel syndrome (IBS), antidiarrheal agents, antiflatulents, cathartics and laxatives, and antiemetics.
2. List the seven types of laxatives according to use, side effects, precautions and contraindications, and interactions.
3. Identify examples of drugs from each of the eight categories of gastrointestinal (GI) drugs.
4. Explain important patient education for each category of GI drugs.
5. Differentiate causes and treatment of *Helicobacter pylori* and *Clostridium difficile* infections.

According to the National Institutes of Health, 60–70 million people suffer from digestive diseases. Gastrointestinal (GI) drugs covered in this chapter can be divided into the following eight categories based on their mechanism of action:

Antacids
Drugs for treatment of ulcers and gastroesophageal reflux disease (GERD)
GI antispasmodics
Agents for inflammatory bowel disease
Antidiarrheal agents
Antiflatulents
Laxatives and cathartics
Antiemetics

Antacids

Anti means "against," and antacids basically work "against" excessive acid production to reduce harmful effects. Pyrosis, commonly known as heartburn, and *dyspepsia* (acid indigestion) are experienced by up to 40% of the population in the United States at least once a month. **Antacids** act by partially neutralizing gastric hydrochloric acid and are widely available in many over-the-counter (OTC) preparations for the relief of indigestion, heartburn, and sour stomach. Other **antiulcer** agents are discussed later in this chapter. Antacids are also used at times as supplemental agents in the management of esophageal reflux.

Antacid products may contain aluminum, calcium carbonate, or magnesium, either individually or in combination. Most antacids also contain sodium. Sodium bicarbonate alone is not recommended because of flatulence (gas production), metabolic alkalosis, and electrolyte imbalance with prolonged use. Calcium carbonate (for example, Tums) is fast-acting and possesses good neutralizing capacity but may cause constipation and kidney stones if overused.

The choice of a specific antacid preparation depends on palatability, cost, adverse effects, acid-neutralizing capacity, sodium content, and the patient's renal and cardiovascular function. Generally, antacids have a short duration of action, requiring frequent administration. Magnesium and/or aluminum antacids are the most commonly used. Magnesium can cause diarrhea, and aluminum can cause constipation. Therefore, combinations (for example, Maalox, Gelusil, and Mylanta) are frequently used to control the frequency and consistency of bowel movements.

Side effects with the frequent use of antacids may include:

- ❗ Constipation (with aluminum or calcium carbonate antacids)
- ❗ Diarrhea (with magnesium antacids)
- ❗ Electrolyte imbalance
- ❗ Urinary calculi (stone formation) and renal complications
- ❗ Osteoporosis (with aluminum antacids)
- ❗ Belching and flatulence (with calcium carbonate and sodium bicarbonate)

Cautions or contraindications with antacids apply to:

- Heart failure
- Chronic kidney disease or history of renal calculi
- Cirrhosis of the liver or edema
- Dehydration or electrolyte imbalance

Antacids may either increase or decrease the absorption of other medications. Because they may decrease the effectiveness of the drug, antacids should not be taken within 2 h of administering the following medications:

- Anti-infectives, especially tetracyclines, quinolones, and isoniazid
- Digoxin, indomethacin, and iron
- Salicylates and thyroid hormones
- Bisphosphonates (i.e., Actonel, Fosamax)

Patient Education

Patients using antacids should be instructed regarding:

Avoiding prolonged use (no longer than 2 weeks) of OTC antacids without medical supervision because of the danger of masking symptoms of GI bleeding or GI malignancy and causing the stomach to increase acid production further

Avoiding the use of antacids at the same time as any other medication because of many interactions (check with a pharmacist or physician concerning clinically important interactions)

Avoiding the use of antacids entirely or using them with caution if the patient has cardiac, renal, or liver disease or fluid retention

Taking antacids with the following drugs may increase the action of certain drugs and precipitate side effects:

Diazepam, which increases sedation

Amphetamines and quinidine, which increase cardiac irregularities

Enteric-coated drugs, which may be released prematurely in the stomach (separate doses from antacids by 2 h)

Patients taking medication for the management of esophageal reflux should also be instructed regarding avoidance of constrictive clothing, treatment of obesity (if appropriate), reducing meal size, avoiding lying down after meals, restriction of alcohol use, elimination of smoking, and elevating the head of the bed during sleep.

Agents for Treatment of Ulcers and Gerd

H_2 blockers

The histamine receptors found in the stomach are called H_2-receptors. H_2-receptor antagonists *reduce gastric acid secretion* by acting as **histamine$_2$ blockers**. They also reduce the amount of gastric acid released in response to stimuli such as food and caffeine. The drugs in this category are used *short-term* for the relief of "acid indigestion and heartburn," **gastroesophageal reflux disease (GERD)**, esophagitis, and prevention of duodenal ulcer recurrence. Additionally, they are used in the maintenance or long-term relief of the listed disease states but are dosed twice daily or at bedtime. Because they do not provide 24-h relief, they are generally not considered first-line treatment unless proton pump inhibitors (PPIs) (discussed later in the chapter) cannot be taken.

A previously used H_2 blocker, ranitidine, was removed from the market by the FDA in 2022 due to high levels of an impurity called NMDA. It was found that this impurity increased in concentration with extended shelf life at warmer temperatures. All formulations of this medication have been recalled, leaving two H_2 blockers available for use—cimetidine and famotidine.

A newer combination medication, Duexis (famotidine and ibuprofen), is approved for the treatment of arthritis and rheumatoid arthritis. Because ibuprofen and other NSAIDs can cause stomach ulcers, the famotidine (H_2 blocker) acts as a protectant.

Side effects of H_2 blockers, usually transient and dose-related, can include:

❗ Diarrhea, dizziness, rash, and headache

❗ Mild gynecomastia with cimetidine occurs infrequently and is reversible

❗ Mental confusion (especially in older adults or those in a severely weakened state; less with Pepcid)

Cautions or contraindications with H_2 blockers apply to:

Renal disease (may need to reduce dose and/or frequency)
Pregnancy
Lactation

Interactions with cimetidine may occur with increased blood concentrations of:

Warfarin (Coumadin) (also with high doses of Zantac)
Phenytoin
Beta-blockers
Benzodiazepines
Lidocaine
Theophylline (also with high doses of Zantac)
Tricyclic antidepressants
Proton pump inhibitors may interfere with the effectiveness of H_2 blockers; when given together the H_2 blocker is usually given at bedtime

All the H_2 blockers are available OTC for up to two weeks of self-treatment; beyond that time frame a physician should be consulted.

Note

There is less likelihood for drug interactions with Pepcid.

Proton Pump Inhibitors

GERD is caused by the excessive reflux of acidic gastric contents into the esophagus, resulting in irritation or injury to the esophageal mucosa characterized by heartburn and acid regurgitation. Serious complications include esophageal stricture, pulmonary aspiration, and esophageal cancer.

Omeprazole (Prilosec) is a gastric antisecretory agent (**proton pump inhibitor** or **PPI**), unrelated to the H_2-receptor antagonists. It is used for the *short-term* (4 to 8 weeks) symptomatic relief of GERD, for the *short-term* treatment of *confirmed* gastric and duodenal ulcers, and for erosive esophagitis and “heartburn.” PPIs may be used *long-term* for severe GERD, preventing nonsteroidal anti-inflammatory drug (NSAID)-induced ulcers, and hypersecretory conditions. Other drugs in this category include lansoprazole (Prevacid), rabeprazole (Aciphex), pantoprazole (Protonix), esomeprazole (Nexium), and dexlansoprazole (Dexilant).

Side effects of PPIs can include:

❗ Diarrhea, constipation, nausea, vomiting, and abdominal pain

❗ Increased risk for pneumonia or intestinal (*Clostridium difficile*) infection

Long-term use on a regular basis of agents that reduce gastric acid can possibly result in vitamin B_{12} deficiency and low magnesium levels in the blood, especially in older adults.

In patients older than 50 years, long-term PPI therapy (at least one year), particularly at high doses, is also associated with an increased risk of hip, wrist, or spine fractures. A potential mechanism for this is PPIs’ interference with calcium absorption.

Long-term use can also increase the risk of Alzheimer’s disease in older adults.

Note

PPIs available as slow-release (SR) tabs should *not* be chewed, broken, or crushed. PPIs available as SR caps may be opened and sprinkled on applesauce or yogurt, given with fruit juices, and swallowed immediately with water (do not chew or crush). Zegerid is an immediate-release product.

Interactions of PPIs may occur with:

H_2 blockers (decrease PPI effectiveness)

Sucralfate (delays absorption of most PPIs)

Benzodiazepines, phenytoin, and warfarin (increased serum levels)

Ampicillin, ketoconazole, iron salts, vitamin B_{12}, bisphosphonates (results in poor bioavailability)

Food—Nexium, Prevacid, and Prilosec should be given on an empty stomach; Aciphex and Protonix can be given without regard to meals.

Clinical Application

Gastric vs. Duodenal Ulcer

Ulcers are a common condition that can affect any patient, although they increase with age, and are more common in those hospitalized and in females. The most common symptom of both gastric and duodenal ulcers is epigastric pain that is characterized by a dull or burning sensation. Whereas people with gastric ulcers tend to exhibit this pain shortly after eating, pain from duodenal ulcers tends to occur a few hours after eating as the food has now entered the small intestine area. If patients suspect they have an ulcer, it is important to determine if the likely cause is *Helicobacter pylori* or from chronic NSAID use. If the patient is a chronic NSAID user, then this is most likely the cause; if they are not chronically using NSAIDs, *H. pylori* is most likely the cause. One can be tested noninvasively for *H. pylori* using a fecal antigen test, or invasively using an endoscope and a rapid urease test. Treatment of *H. pylori* ulcers usually involves a PPI, two or more antibiotics, and a bismuth-based medication to coat the stomach. For NSAID-induced ulcers, it is important to discontinue the NSAID, or if this is not clinically possible, to initiate chronic PPI and/or H_2 antagonist therapy for at least one year. In either case, timely initiation of therapy is important to prevent further complications, which can include internal bleeding or the development of a gastric malignancy (cancerous tissue).

Learning Hint

It may be confusing to understand why H_2-blockers and PPIs have different durations of action when they are acting on the same type of cell. H_2 blockers are generally considered to provide a variable 12 h of relief, while PPIs (when taken daily) provide around-the-clock, more consistent, 24-h, relief. The key to remembering this is that H_2 blockers bind *reversibly* to the histamine receptors directly inside the stomach, which means they can eventually be displaced by histamine, causing the receptor to again be activated. PPIs, on the other hand, are absorbed into the bloodstream, and then bind to the actual proton pumps of the stomach in an *irreversible* manner. This means that they cannot be displaced and the body must create a new pump. In general, this process takes 24 h.

Gastric Mucosal Agents

Misoprostol (Cytotec)

Misoprostol (Cytotec), a synthetic form of prostaglandin E_1, inhibits gastric acid secretion and protects the mucosa from the irritant effect of certain drugs, for example, NSAIDs, especially in those at risk, for example, those in a severely weakened state, older adults, or those with a history of gastric ulcers. Prophylactically, it is approved to prevent NSAID-induced ulcers and can be used off label to treat gastric ulcers when patients are unable to take other medications. It is also commonly used during pregnancy to induce labor or terminate pregnancy.

Side effects of Cytotec can include:

! Diarrhea, nausea, and abdominal pain (occurs early in the treatment and is usually self-limiting; take with food to minimize effects)

Menstrual irregularities (begin therapy on the second or third day of the next normal menstrual period)

Cautions or contraindications for Cytotec include:

Females of childbearing age (unless the female is capable of using effective contraceptives)

Pregnant persons (unless attempting to induce labor or terminate pregnancy)

Children under age 12

Interactions with antacids decrease the rate of absorption. Therefore, it is recommended that antacids be given at least 2 h away and should not be of a magnesium type (which exacerbates diarrhea).

Sucralfate (Carafate)

Sucralfate (Carafate), an inhibitor of pepsin, is another antiulcer agent that acts in a different way. Sucralfate is *administered on an empty stomach* and then reacts with hydrochloric acid in the stomach to form a paste that adheres to the mucosa, thus protecting the ulcer from irritation. The therapeutic effects of the drug result from local (i.e., at the ulcer site) rather than systemic activity.

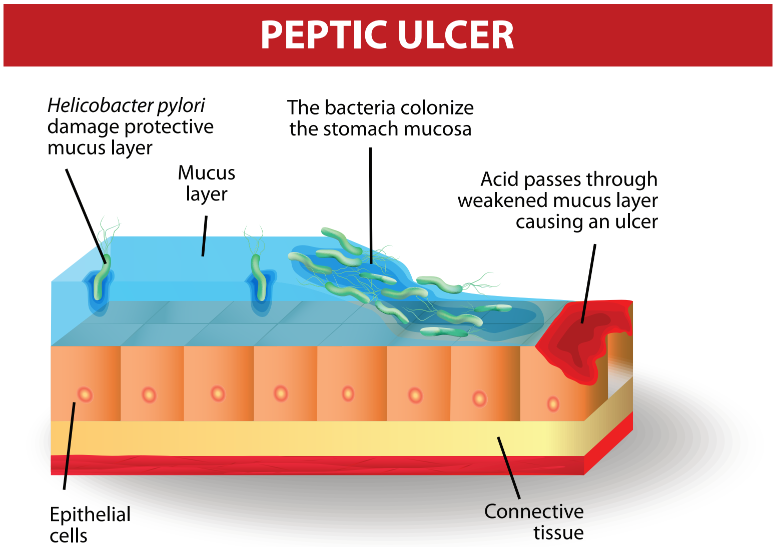
Side effects of sucralfate are rare, with constipation occurring occasionally.

Interactions are possible, with sucralfate altering absorption of certain drugs. Avoid giving other drugs within 2 h of sucralfate, especially antibiotics and antacids.

Antacids may decrease binding of sucralfate to mucosa, decreasing effectiveness. Separate administration times by 30 min.

Helicobacter pylori Treatment

Helicobacter pylori bacterial infection plays a major role in the development of gastritis, gastric and duodenal ulceration, and gastric cancer (Figure 16-1).


PEPTIC ULCER
Helicobacter pylori damage protective mucus layer
The bacteria colonize the stomach mucosa
Mucus layer
Acid passes through weakened mucus layer causing an ulcer
Epithelial cells
Connective tissue

Designua/www.Shutterstock.com.

Figure 16-1 The mechanism by which a *Helicobacter pylori*-induced ulcer is formed. In NSAID-induced ulcers it is the same, but NSAIDs inhibit the mucosal layer from forming around the stomach and can also irritate the gastric lining.

Patient Education

Patients undergoing ulcer therapy should be instructed regarding:

- Avoiding cigarette smoking, which seems to decrease the effectiveness of medicines in the healing of duodenal ulcers
- Importance of close communication with the physician for possible dosage regulation of other medications taken at the same time
- Structuring of the environment to reduce stress factors and decrease tension to facilitate the healing of ulcers
- Not taking antacids within 2 h of any other drug
- Taking medications on a regular basis and avoiding abrupt withdrawal, which could lead to rebound hypersecretion of gastric acid
- Taking sucralfate (Carafate) 1 h before meals, on an empty stomach, and not within 2 h of any other medicine
- Taking misoprostol (Cytotec) with meals and at bedtime with food, and avoiding magnesium products to lessen the incidence of diarrhea
- Taking PPIs, esomeprazole (Nexium), lansoprazole (Prevacid), and omeprazole (Prilosec) on an empty stomach; rabeprazole (Aciphex), dexlansoprazole (Dexilant), and pantoprazole (Protonix) can be given without regard to meals
- That self-medication with OTC PPIs is not intended for *immediate relief* of heartburn
- PPIs available as delayed-release dosage forms should *not* be chewed, broken, or crushed

Helicobacter pylori has been treated successfully with multiple-drug regimens (over 14 days).

Table 16-1 lists antacids, agents for ulcers and GERD, and protective gastric mucosal medications.

Table 16-1 Antacids, Antiulcer Agents, and Gastric Mucosal Agents

Generic Name	Trade Name	Dosage
Antacids (Only a Sample; Many Other Products Are Available)		
aluminum hydroxide gel		Suspension, 600 mg per 5 mL between meals and hs
calcium carbonate	Tums	Tabs, 500–2,000 mg orally in two to four divided doses daily
aluminum–magnesium combinations with simethicone	Maalox, Gelusil, Mylanta	Suspension, tabs; dose varies with product
Agents for Ulcers and GERD		
H_2-Blockers		
cimetidine		300 mg q6 h PO
	Tagamet HB (OTC)	200 mg daily bid PO (2 weeks max)
famotidine	Pepcid	20 mg bid or at bedtime; 40 mg PO tabs at bedtime
		20 mg IV diluted q12h
	Pepcid AC (OTC)	20 mg daily or 10 mg bid (2 weeks max)
with calcium carbonate and magnesium hydroxide	Pepcid Complete (OTC)	One to two tabs daily
with ibuoprofen	Duexis	800 mg/26.6 mg q8h

Generic Name	Trade Name	Dosage
Proton-Pump Inhibitors		
dexlansoprazole	Dexilant	30–60 mg daily taken without regard to food
esomeprazole	Nexium	20–40 mg ac daily SR caps, susp, IV diluted
lansoprazole	Prevacid	15–30 mg ac daily SR caps,
		SoluTab; 30 mg daily IV diluted
	Prevacid 24 HR (OTC)	15 mg daily, SR caps (2 weeks max)
omeprazole	Prilosec	20–40 mg qAM ac, SR caps, susp
	Prilosec OTC	20 mg daily ac SR tab (2 weeks max)
with sodium bicarbonate	Zegerid	20–40 mg ac daily caps, susp
	Zegerid OTC	20 mg ac daily caps (2 weeks max)
pantoprazole	Protonix	20–40 mg orally daily SR tabs, susp; 40 mg daily IV diluted
rabeprazole	Aciphex	20 mg daily SR tab
Gastric Mucosal Agents		
misoprostol	Cytotec	100–200 mcg four times per day with meals and at bedtime with food
sucralfate	Carafate	1 g four times per day (1 h ac and at bedtime), tabs, susp

Note: PPIs can be dosed bid in cases where daily dosing improves symptoms but does not last 24 h.

GI Antispasmodics or Anticholinergics

Dicyclomine

Antispasmodics or anticholinergics help to calm the bowel. Dicyclomine (Bentyl) is an anticholinergic and antimuscarinic agent used for the treatment of irritable bowel syndrome and other functional disturbances of GI motility. GI anticholinergics work by decreasing motility (smooth muscle tone) in the GI tract.

Side effects of dicyclomine, especially in older adults, can include:

❗ Dry mouth and constipation
❗ Blurred vision, dizziness, and drowsiness
❗ Urinary retention (decreases smooth muscle tone in the urinary tract)
Tachycardia, palpitations
❗ Confusion (especially in older adults)

Cautions or contraindications of dicyclomine include:

Glaucoma (narrow angle)
Unstable cardiac disease
Obstructive GI disease and ulcerative colitis

Obstructive uropathy (benign prostatic hyperplasia [BPH] and bladder obstruction)

Myasthenia gravis

Lactation

Interactions of dicyclomine include:

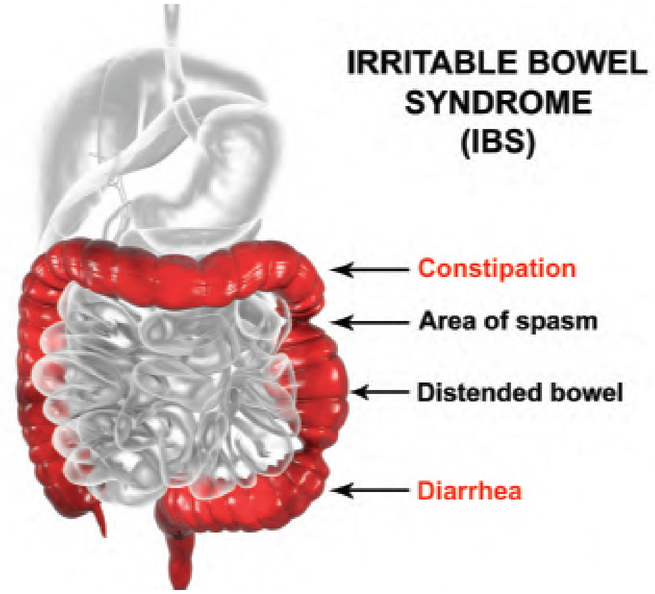
Phenothiazines (decreased antipsychotic effectiveness, increased anticholinergic side effects)

Tricyclic antidepressants (increased anticholinergic side effects)

Opiate agonists (additive depressive effects on GI motility or bladder function)

Agents for Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a *chronic* condition that causes inflammation in the lining of the GI tract and includes Crohn's disease and ulcerative colitis. One of the main clinical features of this condition is abnormal defecation, which may be predominantly constipation or diarrhea. There is no cure for IBD, and treatment strategies focus on symptom control and improvement in the quality of life. Because IBD is generally caused by inflammation of the colon or muscle spasms throughout the colon, treatment is intended to minimize these occurrences and the severity of them. Refer to Figures 16-2 and 16-3 for a review of both disease states, but understand that each case of Crohn's disease and ulcerative colitis is unique and can vary greatly from patient to patient.

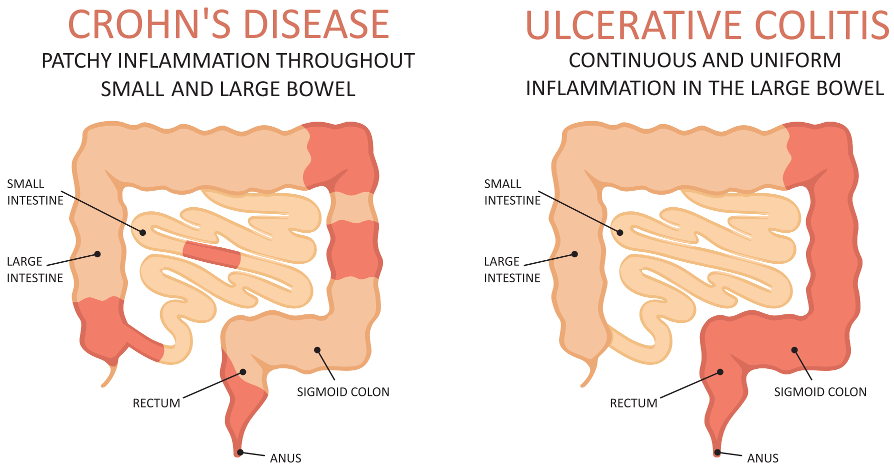


Kateryna Kon/Shutterstock.com.

Figure 16-2 Irritable bowel syndrome (IBS).

Constipation: Occurs most commonly if irritation of spasm occur in the ascending or upper part of the colon.

Diarrhea: Occurs most commonly if irritation of spasm occur in the descending or lower part of the colon.


CROHN'S DISEASE
PATCHY INFLAMMATION THROUGHOUT SMALL AND LARGE BOWEL
SMALL INTESTINE
LARGE INTESTINE
RECTUM
SIGMOID COLON
ANUS
ULCERATIVE COLITIS
CONTINUOUS AND UNIFORM INFLAMMATION IN THE LARGE BOWEL
SMALL INTESTINE
LARGE INTESTINE
RECTUM
SIGMOID COLON
ANUS

logika600/Shutterstock.com.

Figure 16-3 Contrast of Crohn's disease and ulcerative colitis.
UC and CD: As disclaimer that both UC and CD can cause diarrhea or constipation.

Salicylates

Mesalamine (Asacol, Rowasa) and the prodrug sulfasalazine (Azulfidine) have chemical structures similar to that of aspirin and exhibit anti-inflammatory activity in the GI tract. They are used in the management of Crohn's disease and ulcerative colitis. These salicylates are all designed to reach the ileum and colon, bypassing the stomach and upper intestines. They are safe for long-term use and are well tolerated in most patients.

Side effects of salicylates (often more frequent and severe with sulfasalazine) can include:

- ❗ Anorexia, nausea, vomiting, diarrhea, and dyspepsia
- ❗ Abdominal pain, cramps, and bloating (with rectal administration)
- ❗ Headache, weakness, dizziness, and rash

  Intolerance to sulfasalazine can be minimized by taking the enteric-coated product (Azulfidine EN-tabs).

Cautions and contraindications with sulfasalazine apply to those having:

- ❗ Allergy to salicylates
- ❗ Allergy to sulfonamides with sulfasalazine (can cause anaphylaxis or asthma attacks)
- ❗ Allergy to sulfites (Rowasa enema)
- Renal impairment
- Hepatic impairment (with sulfasalazine)

Interactions with sulfasalazine include:

- Warfarin (increased risk of hemorrhage)
- Methotrexate (increased bone marrow suppression)
- Cyclosporine (decreased efficacy)
- Oral diabetic agents (hypoglycemia)
- Folic acid (absorption is inhibited)

Glucocorticoids

Glucocorticoids (prednisone, prednisolone, and hydrocortisone enema) are used to treat moderate to severe *active* forms of IBD in patients who are inadequately controlled with salicylates. The oral steroids do not require direct contact with the inflamed intestinal tissue to be effective.

Monoclonal Antibodies

Monoclonal antibodies can be used to treat refractory and severe cases of Crohn's disease and other forms of IBD. While there are many that have been recently approved for this use, all function to decrease the body's inflammatory response and decrease symptoms. Patients taking monoclonal antibodies are at a higher risk of infection and should not receive live vaccines. These medications are administered via subcutaneous injection or intravenous infusion.

Side effects of monoclonal antibodies:

Upper respiratory infections
Injection site pain
Urinary tract infections
Allergic reactions

Cautions and contraindications of monoclonal antibodies:
Increased risk of serious infections such as tuberculosis, invasive fungal infections

GC-C agonists

Linaclotide (Linzess) is a medication that is indicated for IBD with severe constipation. It is a once daily oral capsule that works by activating GC-C receptors on the inside of the epithelial lining. This causes an increase in fluid secretion and therefore an increase in bowel motility. Linaclotide is not absorbed systemically, so side effects are limited to the gastrointestinal system.

Side effects of GC-C agonists:

Diarrhea, abdominal pain, flatulence

Cautions and contraindications of GC-C agonists:

Contraindicated in patients under 6 years old
Contraindicated if bowel obstruction present
Caution use in patients 6–18 years old

Antidiarrheal Drugs

Antidiarrheal agents act in various ways to reduce the number of loose stools. Patients who are experiencing diarrhea should be instructed to stay hydrated with fluids such as water and electrolyte solutions such as Pedialyte. Sports drinks and sodas should not be used because of high sugar content, which can dehydrate the body further and worsen diarrhea.

Bismuth Subsalicylate

Bismuth subsalicylate (e.g., Kaopectate, Pepto-Bismol) has anti-infective and antisecretory properties, a direct mucosal protective effect, and weak antacid and anti-inflammatory effects. Kaopectate brand products have been reformulated several times over the years. Be aware that several formulations of “generic” Kaopectate are still available—check label contents and dosing carefully.

Side effects of bismuth subsalicylate are relatively uncommon at normal doses and include:

❗ Transient, occasional constipation

❗ Discoloration of tongue and stool (black color)

Ringing in ears

Interactions with bismuth subsalicylate are possible when these agents are administered concurrently with medications such as:

Warfarin (increases bleeding)

Aspirin and methotrexate (increases toxicity)

Quinolones and tetracyclines (decreases bioavailability)

Cautions or contraindications for bismuth subsalicylate include:

Salicylate (including aspirin) hypersensitivity

Children (<12 years old) or adolescents recovering from chickenpox or influenza (risk of Reye’s syndrome)

Coagulation abnormalities and ulcers

Pregnancy and lactation

Patient Education

Patients treated with bismuth subsalicylate should be instructed regarding:

Avoiding self-medication for longer than 48 h or if fever develops

Diet of a bland nature, excluding roughage and including foods containing natural pectin (e.g., apple *without* peel and without sugar added)

Adequate fluid intake (especially tea *without* sugar for its astringent effect) or intake of oral electrolyte products (e.g., Gatorade, Pedialyte) to prevent dehydration

Contacting the physician immediately if complications develop or condition worsens and if observing blood in stool

Not using bismuth subsalicylate if allergic to salicylates (including aspirin) and in children or adolescents recovering from chickenpox or influenza

Considering all sources of salicylate if taking aspirin or other medications containing salicylate, so that toxic levels are not reached

Opiate Agonists: Diphenoxylate with Atropine and Loperamide

These products act by slowing *intestinal motility*, thus allowing for more reabsorption of fluid back into the body and therefore solidifying the feces. Lomotil is a product combining diphenoxylate with atropine. It is a Schedule C-V controlled substance. Loperamide (Imodium) is available in various forms; all are OTC products, except for some capsule formulations, which remain prescription only (refer to Table 16-2).

Side effects can include:

❗ Anticholinergic effects with Lomotil (e.g., drying of secretions, blurred vision, urinary retention, lethargy, confusion, or flushing)

❗ Abdominal distention, nausea, or vomiting with Lomotil or Imodium

Cautions or contraindications include:

Diarrhea caused by infection or poisoning
Fever over 101°F
Young children (under 3 years of age)
Pregnancy
Clostridium difficile colitis associated with antibiotics
Obstructive jaundice

Cautions or contraindications apply to older adults.

Probiotics

Probiotics are living microorganisms that can alter a patient's intestinal flora and may provide benefit in numerous GI diseases. The body's naturally occurring gut flora may fall out of balance in a wide range of circumstances, including the use of antibiotics or other drugs, excess alcohol, stress, certain diseases, or exposure to toxic substances.

Patient Education

Patients taking antidiarrheal drugs should be instructed regarding:

Not exceeding the recommended dosage; short-term (48 h) only
Adequate fluid intake and bland diet
Reporting side effects or complications to the physician immediately, or if symptoms persist or worsen
Not taking these medications if diarrhea is caused by infection or food poisoning

Lactobacillus acidophilus is an acid-producing probiotic bacterium, available in several forms OTC. It is administered orally for the *treatment* of simple uncomplicated diarrhea caused by antibiotics, infection, irritable colon, colostomy, or amebiasis. *Lactobacillus* bacteria help to reestablish normal intestinal flora. The capsules, tablets, powder, or granules may be taken directly or mixed with cereal, food, milk, juice, or water.

Side effects tend to be mild and digestive (gas, bloating) in nature.

Cautions or contraindications for *Lactobacillus* apply to:

Anyone with a high fever; weakened immune system
Those sensitive to milk products or with a lactase deficiency
Long-term use, unless directed by the physician
Patients with prosthetic heart valves or valvular heart disease (risk of bacteremia)

Saccharomyces boulardii (Florastor) is a yeast used in dairy fermentation. It is derived from the intestinal microbiota of healthy humans. It is a probiotic often started within 3 days of antibiotic initiation and continued for 3 days after discontinuation to *prevent* diarrhea. Probiotic bacteria are also found in yogurt (Activia) and other dairy foods for the replacement of beneficial intestinal tract bacteria.

There are many other available probiotic bacteria available OTC, and patients should be instructed to use a trial-and-error method of choosing an appropriate option.

Clostridium difficile Infection

Clostridium difficile is one of the most common causes of infectious diarrhea in the United States. Symptoms of *C. difficile* diarrhea (CDD) may include watery diarrhea, nausea, and/or abdominal pain or tenderness. Complications may include sepsis, renal failure, toxic colitis, and death. CDD is caused primarily by the eradication of the native intestinal flora with broad-spectrum antimicrobials and overuse of PPI and H_2 blocker therapy. Please refer to Figure 16-4 for special considerations related to patients with *C. difficile*.

PhotoMediaGroup/Shutterstock.com.

Figure 16-4 When a patient is hospitalized and diagnosed with *Clostridium difficile* they are moved to a contact isolation room to prevent the spread of infection. Barrier precautions such as this gown and thorough handwashing are very important. Alcohol-based hand sanitizers do not eliminate the *C. difficile* spores.

Oral medications include metronidazole (Flagyl) and vancomycin. Opiates and antidiarrheal medications may decrease GI motility, thereby increasing toxins in the intestine, so their use *should be avoided*.

Antiflatulents

Antiflatulents (e.g., simethicone) are used in the symptomatic treatment of gastric bloating and postoperative gas pains by helping to break up gas bubbles in the GI tract.

Cautions or contraindications apply only to infant colic because of limited information on safety in children.

Table 16-2 provides a summary of antispasmodic, IBD, antidiarrheal, and antiflatulent agents.

Patient Education

Patients should be instructed to avoid gas-forming foods (e.g., onions, cabbage, and beans).

Table 16-2 GI Antispasmodic, IBD, Antidiarrheal, and Antiflatulent Agents

Generic Name	Trade Name	Dosage
GI Antispasmodics or Anticholinergics		
dicyclomine	Bentyl	PO 20–40 mg four times per day caps, tabs; IM 20 mg q6h (2 days max; switch to PO)
Agents for IBD		
Salicylates		
mesalamine	Asacol HD	2 × 800 mg PO tid (up to 6 weeks), DR tab
	Rowasa	4 g R at bedtime (retain 8 h; use 3 to 6 weeks), enema
	Canasa	1,000 mg R at bedtime (retain 1–3 h; use 3 to 6 weeks), suppository
sulfasalazine	Azulfidine	500 mg tab or DR tab
	Azulrfidine EN-tab	500 mg–1 g four times per day
Monoclonal Antibodies (Representative List)		
adalimumab	Humira	40 mg SC q2w
infliximab	Remicade	5 mg/kg IV q8w
GC-C agonists		
linaclotide	Linzess	72 mcg, 145 mcg, 290 mcg daily
Antidiarrheal Agents		
Salicylates		
bismuth subsalicylate	Kaopectate, Pepto-Bismol	Susp, 30 mL or 2 tabs q30–60 min after each BM (max eight doses per day)
Opiate agonists		
diphenoxylate with atropine	Lomotil	Sol or tabs, 2.5–5 mg four times per day (max 20 mg per day)
loperamide	Imodium caps (Rx)	Sol, tabs, caps; 4 mg initially, 2 mg after each loose BM until stools are solid
	Imodium A-D (OTC)	(Rx maximum 16 mg per day; OTC maximum 8 mg per day × 2 days)
Probiotics Representative List		
Lactobacillus acidophilus	Lactinex, Bacid	2 caps, 4 tabs, or 1 pkg granules three or four times per day
Lactobacillus GG	Culturelle	1 cap PO bid (continue for 1 week after discontinuation of antibiotics)
Saccharomyces boulardii	Florastor	2 caps PO bid (start within 3 days of antibiotic; continue for 3 days after discontinuation)
Antiflatulent		
simethicone	Mylicon	Liquid, tabs pc, and at bedtime 160–500 mg daily in divided doses

Laxatives and Cathartics

Laxatives promote evacuation of the intestine and are used to treat constipation. Included in the laxative category are *cathartics*, or *purgatives*, which promote *rapid evacuation* of the intestine and alteration of stool consistency (stool softener to make it easier to flow). Laxatives can be subdivided into seven categories according to their action: bulk-forming laxatives, stool softeners, emollients, saline laxatives, stimulant laxatives, osmotic laxatives, and chloride channel activator.

Many OTC laxatives are self-prescribed and overused by a large portion of the population. Prevention and relief of constipation is better achieved through natural methods (e.g., high-fiber diet, adequate fluid intake, good bowel habits, and exercise). Normal frequency of bowel movements varies from daily to several times weekly. When constipation occurs, the cause should be identified before laxatives are used.

Bulk-Forming Laxatives

Bulk-forming laxatives, also known as fiber supplements (e.g., psyllium, cellulose derivatives, polycarbophil, and bran), soften the stool by absorbing water and increase fecal mass to facilitate defecation. They are the treatment of choice for simple constipation unrelieved by natural methods. These products are available in powders, capsules, tablets, and wafers and *must be dissolved* or *diluted* according to manufacturers' directions (note label). The usual procedure is to take or dissolve the product in one *full glass* of water or juice to be taken orally and followed immediately with another glass of fluid. The proper dosage is administered one to three times per day. Laxative effect is usually apparent within 12–72 h.

Bulk-forming laxatives are the choice for older adults and patients who are laxative-dependent. They have been useful in maintaining regularity for patients with diverticulosis and in increasing the bulk of stools in patients with chronic watery diarrhea.

Cautions or contraindications for bulk-forming laxatives apply to patients with acute abdominal pain, partial bowel obstruction, dysphagia (difficulty in swallowing), or esophageal obstruction.

Patient Education

Patients should be instructed regarding:

Dissolving all bulk-forming products completely in one full glass of liquid and following that with another glass of fluid to prevent obstruction

Administering immediately when dissolved, before thickening occurs

Stool Softeners

Stool softeners (e.g., docusate) are surface-acting agents that moisten stool through a detergent action and are administered orally. The dosage required to soften stools varies widely depending on the condition and patient response. Stool softeners are the choice for pregnant persons or persons who are nursing and children with hard, dry stools. The onset of action is usually 12–72 h.

Side effects are rare, with occasional mild, transitory GI cramping or rash.

Cautions or contraindications apply to acute abdominal pain or prolonged use (more than 1 week) without medical supervision.

Caution to avoid stool softeners that also contain stimulant laxatives, for example, Peri-Colace, Senokot-S.

Patient Education

Patients taking stool softeners should be instructed regarding:

- Discontinuance with any signs of diarrhea or abdominal pain
- Avoiding use for longer than 1 week without medical supervision
- Interaction with mineral oil, which leads to mucosal irritation and systemic absorption of mineral oil
- Taking large quantities of fluids to soften stool
- Checking package labels to be sure no cathartics are included

Emollients

Emollients promote stool movement through the intestines by softening and coating the stool. Mineral oil may be administered orally and is usually effective in 6–8 h. Mineral oil is sometimes administered rectally as an oil-retention enema (60–120 mL).

Side effects of emollients may include:

- ❗ Seepage of oil from rectum, causing anal irritation
- ❗ Malabsorption of vitamins A, D, E, and K only with prolonged oral use

Cautions or contraindications for oral mineral oil apply to:

- Children under 5 years old
- Nonambulatory patients who spend the majority of their time in bed, those in a severely weakened state, or older adult patients
- Patients with dysphagia, gastric retention, or hiatal hernia
- Pregnancy
- Prolonged use
- Concomitant use of stool softeners

Patient Education

Patients taking mineral oil should be instructed regarding:

- Avoiding frequent or prolonged use
- Using caution if having trouble swallowing or with aspiration of the oil (potential of lipoid pneumonitis if aspirated); never take mineral oil at bedtime
- Interaction with docusate (stool softener), which can facilitate absorption of mineral oil, possibly increasing the risk of toxicity

Saline Laxatives

Saline laxatives (e.g., milk of magnesia [MOM] or citrate of magnesia) promote secretion of water into the intestinal lumen (opening) and should be taken only infrequently in single doses. Saline laxatives should not be taken on a regular or repeated basis unless directed by a physician. The onset of action is 0.5–3 h.

Side effects of saline laxatives used for prolonged periods or in overdoses can include:

- ❗ Electrolyte imbalance
- ❗ CNS symptoms, including weakness, sedation, and confusion
- ❗ Edema
- ❗ Cardiac, renal, and hepatic complications

Cautions or contraindications apply to:

- Long-term use
- Heart failure or other cardiac disease
- Edema, cirrhosis, or renal disorders
- Those taking diuretics
- Acute abdominal pain
- Colostomy

Patient Education

Patients taking saline laxatives should be instructed regarding:

- Using caution as products of different strengths are available (MOM comes in 400, 800, and 1,200 mg per 5 mL concentrations)
- Avoiding saline cathartics with certain medical conditions
- Avoiding frequent or regular use of saline cathartics

Stimulant Laxatives

Stimulant laxatives (e.g., senna, castor oil, and bisacodyl) are cathartic in action, producing strong peristaltic activity, and may also alter intestinal secretions in several ways. Stimulant laxatives are habit-forming, and long-term use may result in laxative dependence and the loss of normal bowel function. All stimulant laxatives produce some degree of abdominal discomfort. Their use should be confined to conditions in which rapid, thorough emptying of the bowel is required (e.g., before surgical, proctoscopic, sigmoidoscopic, or radiological examinations, or for emptying the bowel of barium following GI X-rays) or for patients on opioid therapy. Sometimes a combination of oral preparations, suppositories, and/or enemas may be ordered for these purposes. The onset of action is 0.25–8 h, depending on the preparation.

Side effects of stimulant laxatives are common, especially with frequent use, and can include:

- ❗ Abdominal cramps or discomfort and nausea (frequent)
- Rectal and/or colonic irritation with suppositories
- ❗ Loss of normal bowel function with prolonged use

❗ Electrolyte disturbances and dehydration with prolonged use
Discoloration of urine with senna

Cautions or contraindications with stimulant laxatives apply to:

- Acute abdominal pain or abdominal cramping—danger of ruptured appendix
- Ulcerative colitis
- Children and pregnant persons and persons lactating
- Long-term use

Patient Education

Patients taking stimulant laxatives should be given strong warnings against frequent or prolonged use because of the danger of laxative dependence and loss of normal bowel function.

Because of gastric irritation, bisacodyl tablets should not be crushed or chewed, or taken within 1 h after milk or antacids.

Osmotic Laxatives

Osmotic laxatives such as glycerin, lactulose, polyethylene glycol (PEG), and sorbitol exert an action that draws water from the tissues into the feces and reflexively stimulates evacuation. Response and side effects vary with preparation. Lactulose response may take 24–48 h. Side effects include nausea, vomiting, flatulence, and abdominal cramps. Osmotic laxatives are also used to treat encephalopathy (brain and nervous system damage) in hepatic failure precipitated by GI bleeding and other conditions.

Glycerin rectal suppositories or enemas usually cause evacuation of the colon within 15–60 min. Glycerin may produce rectal irritation or cramping pain. Polyethylene glycol (Miralax) response can be seen in 0.5–3 h; however, 2 to 4 days of therapy may be required to produce a bowel movement. Side effects are similar to other drugs in this category; high doses of Miralax can cause electrolyte imbalances (hyponatremia, hypokalemia) with prolonged or excessive use.

Chloride Channel Activators

Lubiprostone (Amitiza) is a unique oral agent for the treatment of constipation. It increases intestinal fluid secretion by activating specific chloride channels in the intestinal epithelium. Lubiprostone alters stool consistency and promotes regular bowel movements without altering electrolyte balance or producing tolerance. Most patients experience a bowel movement within 24 h of the first dose.

Side effects of lubiprostone can include:

❗ Nausea and diarrhea
Headache
Abdominal bloating or pain and flatulence

Cautions or contraindications apply to:

- Severe diarrhea or bowel obstruction
- Renal or hepatic impairment
- Pregnancy and breast feeding

Patient Education

Patients with constipation issues should be instructed regarding:

- High-fiber diet to prevent constipation, including roughage (e.g., bran, whole-grain cereals, and fresh fruits and vegetables)
- Adequate fluid intake
- Developing good bowel habits (e.g., regular, at an unrushed time of day)
- Regular exercise to develop muscle tone
- Avoiding laxatives if the patient is experiencing acute abdominal pain, nausea, vomiting, or fever
- Avoiding laxatives if any medical condition is present, unless prescribed by a physician; bulk-forming laxatives are safest in the long term
- Using only the mildest laxatives (e.g., stool softeners) on a short-term, infrequent basis
- Reporting any prolonged constipation, if treatment is ineffective, to a physician for investigation

Peripherally Acting Mu-opioid Receptor Antagonists

Naloxegol (Movantik) is an oral agent specifically designed for the treatment of constipation caused by chronic or acute opioid use. It works by acting on the same mu-receptors that opioids do, but selectively inhibits the mu-receptors in the stomach. This action reduces or eliminates the opioid-induced delay in GI transit time caused by opioid stimulation that leads to constipation. It does not have action at other mu-receptors in the body, which means the analgesic properties of the opioid in use remain the same. Other drugs approved in this class are methylnaltrexone (Relistor) and naldemedine (Symproic).

At one time, naloxegol was a Drug Enforcement Administration (DEA) Schedule II medication due to its structural relationship to opioids, but it has since been determined that there is no potential for abuse because peripherally acting mu-opioid receptor antagonists do not cross the blood–brain barrier and it was therefore removed from this schedule. Other drugs in this class remain noncontrolled substances.

Side effects of peripherally acting mu-opioid receptor antagonists can include:

- ❗ Nausea and diarrhea
- Flatulence

Cautions or contraindications with peripherally acting mu-opioid receptor antagonists apply to:

- Severe GI obstruction
- Patients with disruption to blood–brain barrier: may experience withdrawal-like symptoms
- Severe hepatic impairment
- Myocardial infarction with long-term use (with Entereg only)

Interactions may occur with:

- CYP3A4 inhibitors, which increase concentration of naloxegol

Table 16-3 provides a summary of laxatives.

Patient Education

Patients taking Movantik should be instructed to:

- Take on an empty stomach 1 h before first meal of the day or 2 h after
- Avoid grapefruit or grapefruit juice
- Swallow tablets whole; do not crush, split, or chew
- Do not take other laxative medications while on this medication
- Discontinue medication when or if opioid medication is discontinued

Table 16-3 Laxatives

Generic Name	Trade Name	Dosage
Laxatives (Only an Example, Many Other Products Available)		
Bulk-Forming		
psyllium	Metamucil, Konsyl-D, others	Powder, 1–3 tsp, dissolved in or 2–6 caps taken with full glass of fluid one to three times per day
Stool Softener		
docusate	Colace, others	Oral caps, tabs, liquid 50–300 mg daily
Emollient		
mineral oil	Fleet mineral oil	15–45 mL PO daily; 60–120 mL R daily
Saline Laxative		
magnesium hydroxide	Milk of Magnesia	Susp, 15–60 mL daily
Stimulant Laxatives		
senna	Senokot	8.6 mg tab, 1–4 bid or 10–15 mL syrup bid
with docusate	Peri-Colace, Senokot-S	1–2 tabs daily–bid
bisacodyl	Dulcolax	5–15 mg DR tabs, 10 mg suppository
	Fleet	10 mg/30 mL enema
Osmotic Laxatives		
glycerine	Fleet suppository	1 suppository R PRN
lactulose	Enulose	15–60 mL PO daily (10 g/15 mL) (more frequently for hepatic encephalopathy)
polyethylene glycol	Miralax (OTC) GlycoLax (Rx)	17 g (1 capful) in 4–8 oz liquid daily (OTC—7 days max; Rx—14 days+)
sorbitol		30–150 mL PO of 70% solution
Chloride Channel Activator		
lubiprostone	Amitiza	8 mcg cap bid with food (IBD with constipation)
Peripherally Acting Mu-opioid Receptor Antagonists		
naloxegol	Movantik	24 mcg cap bid with food (constipation) 12.5–25 mg daily in the morning on an empty stomach (only use 12.5 mg if patient unable to tolerate 25 mg)

Generic Name	Trade Name	Dosage
methylnaltrexone	Relistor	450 mg PO daily 8-12 mg SQ every other day or daily
naldemedine	Symproic	0.2 mg PO daily

Note: This is only a representative sample. Others are available. Always read labels carefully, especially with OTC medications.

Antiemetics

Emesis refers to the action or process of vomiting. **Antiemetics** are used in the prevention or treatment of nausea, vomiting, vertigo, or motion sickness. Many different types of products are available, varying in their actions, the condition treated, and route of administration. Prevention is preferred over treatment of established nausea and vomiting.

Anticholinergics

Motion sickness is mediated by cholinergic and histaminic receptors in the inner ear. For prophylaxis of motion sickness, anticholinergic drugs such as dimenhydrinate (Dramamine) or scopolamine are used. For greatest effectiveness, the Transderm-Scop patch is applied behind the ear 4 h before anticipated exposure to motion (do not cut patch) and is effective up to 72 h. Dramamine is administered orally 30 min before exposure to motion. Both of these drugs are also available for IM injection in patients who have already developed motion sickness.

Meclizine (Antivert) is an antihistamine used in the prevention and treatment of nausea, vomiting, and/or vertigo associated with motion sickness, and in the symptomatic treatment of vertigo associated with the vestibular system (e.g., Ménière's disease). The onset of action is about 1 h and effects persist 8–24 h after a single oral dose. Although meclizine produces fewer adverse anticholinergic effects (dry mouth, confusion, urinary retention) than scopolamine, it can cause drowsiness, but to a lesser degree than dimenhydrinate (Dramamine). It is not recommended for children under12 years of age.

Antidopaminergics

Dopamine-receptor antagonists interfere with the stimulation of the chemoreceptor trigger zone (CTZ) in the brain, thereby blocking messages to the GI tract. The most frequently used agents to control nausea and vomiting in this class are prochlorperazine (brand name Compazine, which is no longer marketed) and promethazine (Phenergan), which are related to the phenothiazines. These drugs are used for symptomatic relief, and their use must be supplemented by restoration of fluid and electrolyte balance, as well as determination of the cause of vomiting.

Antagonism of dopamine receptors in other areas of the brain, including those involved with movement, can lead to extrapyramidal reactions (tremors, difficulty walking, and muscular rigidity), which are common for drugs in this class at high doses. Prochlorperazine shows a high incidence of extrapyramidal reactions, especially in psychiatric patients receiving phenothiazines long term and in children. It is not recommended for children under 12 years of age. *Caution with older adults. Not for long-term use.*

For *preoperative* preventive antiemetic effect or *postoperative* treatment for nausea and vomiting, promethazine is usually the drug of choice. Promethazine can be given *deep* IM (50 mg/mL concentration only) or via a central line (25 mg/mL concentration only), but *never* subcutaneously due to the risk of serious tissue injury. Metoclopramide (Reglan), a dopamine-receptor antagonist unrelated to other agents, is an antiemetic and a stimulant of upper GI motility. It accelerates gastric emptying and intestinal transit. It is used in a variety of GI motility disorders, especially gastric stasis, *short-term (up to 12 weeks)* treatment of GERD, and prevention (IM/IV only, not oral) of cancer chemotherapy-induced emesis. Extrapyramidal reactions can also occur with metoclopramide.

Serotonin-Receptor Antagonists

Serotonin is a major neurotransmitter that is involved in emesis and is located in the gut. Serotonin-receptor antagonists preferentially block serotonin receptors found centrally in the CTZ and peripherally in the intestines to control emesis. Ondansetron (Zofran), granisetron (Sancuso), dolasetron (Anzemet), and palonosetron (Aloxi) are used for the prevention and treatment of **postoperative nausea and vomiting (PONV)** and for the control of **chemotherapy-induced nausea and vomiting (CINV)**.

These agents have fewer side effects (mainly headache, dizziness, drowsiness, and diarrhea) and are usually well tolerated.

Side effects of the antiemetics vary with the drug and dosage, but the most common include:

- Confusion, anxiety, restlessness (especially in older adults)
- Sedation, drowsiness, vertigo, weakness, and headache
- Diarrhea and depression (with Reglan)
- Dry mouth and blurred vision
- Extrapyramidal reactions (involuntary movements), especially in children and older adults with the antidopaminergics

Cautions or contraindications with antiemetics apply to:

Children and adolescents (increased risk of movement disorders) with antidopaminergics

Pregnancy and lactation

Those in a severely weakened state, emaciated, or older adult patients (require reduced dose)

Angle-closure glaucoma

Prostatic hypertrophy

Cardiac arrhythmias or hypertension

Seizure disorders (seizure threshold lowered)

Chronic obstructive pulmonary disease (COPD) and asthma (Phenergan suppresses cough reflex)

Interactions of antiemetics resulting in the potentiation of a sedative effect occur with:

CNS depressants, including tranquilizers, hypnotics, analgesics, antipsychotics, alcohol, muscle relaxants (potentiation of sedative effects)

Drugs that prolong QT interval (antiarrhythmics, tricyclic antidepressants, phenothiazines, atypical antipsychotics, "mycin" and quinolone antibiotics, and others)

Metoclopramide (other antiemetics also antagonize the stimulant effects of metoclopramide on the GI tract; promethazine can also increase the risk of extrapyramidal reactions if given with metoclopramide)

SSRI antidepressants (*serotonin syndrome* with promethazine and metoclopramide); serotonin syndrome is caused by excess serotonin release, leading to muscle rigidity, increased temperature, changes in blood pressure, confusion, and eventually death

Table 16-4 provides a summary of antiemetics.

Table 16-4 Antiemetics

Generic Name	Trade Name	Dosage
Antiemetics		
Anticholinergics		
dimenhydrinate	Dramamine (PO: OTC; inj: Rx)	50–100 mg PO or IM, IV q4h PRN for motion sickness (max 400 mg PO, 300 mg IM/IV)
meclizine	Dramamine Less Drowsy (OTC)	25–50 mg daily, 1 h before motion (repeat q24h PRN)
	Antivert (Rx)	25–100 mg in divided doses/Ménière's
scopolamine	Transderm-Scop	72-h patch for motion sickness
Antidopaminergics		
metoclopramide	Reglan	PO, IM, IV; dose varies with condition
prochlorperazine	(Compazine)[a]	5–10 mg PO, IM, IV, four times per day; 25 mg suppository bid
promethazine	Phenergan	Tabs, syrup, deep IM, IV, or suppository
		12.5–25 mg (never SQ; caution in older adults)
Serotonin-Receptor Antagonists		
dolasetron	Anzemet	CINV[b]: 100 mg PO; PONV: 12.5 mg IV, 100 mg PO
granisetron	Sancuso	3.1 mg/24-h patch (may wear up to 7 days after chemotherapy)
	Granisol	1 mg/5 mL solution
	Sustol	10 mg/0.4 mL prefilled syringe (extended-release formulation)
ondansetron	Zofran Zofran ODT	CINV: 0.15 mg/kg IV (over 15 min; max 16 mg), 24 mg PO; PONV: 4 mg IM, IV (over 2–5 min), 16 mg PO
palonosetron	Aloxi	CINV: 0.25 mg IV infused over 30 sec PONV: 0.075 mg IV infused over 10 sec

Note: This is only a representative sample. Others are available. Always read labels carefully, especially with OTC medications.

[a] This brand name is no longer marketed, but the name is still commonly used.

[b] Dosage with PONV or CINV

Patient Education

Patients taking antiemetics should be instructed regarding:

- Taking these medications under medical supervision
- Determining the cause of nausea and vomiting
- Reporting effectiveness or complications
- Administering only as directed
- Not combining with any other CNS depressants, SSRI antidepressants, alcohol, or muscle relaxants unless prescribed by a physician (e.g., with cancer patients)

Case Study A

Gastrointestinal Drugs

A 42-year-old-patient called their physician's office to discuss an issue with the nurse. They have had diarrhea for the past 24 h and would like a recommendation for a medication to relieve this condition. They do not have a fever, abdominal pain, cramping, or other symptoms.

1. The nurse suggests that the patient take some Pepto-Bismol, following the medication's label dosages. Which side effect may occur if the patient takes an amount over the recommended dosage?
a. dehydration
b. excessive thirst
c. hypoglycemia
d. black discoloration of the tongue and stool

2. The nurse also reviews what other medications the patient is currently taking. The nurse explains that they should be cautious with which of the following when taking Pepto-Bismol?
a. iron
b. docusate sodium
c. warfarin
d. ibuprofen

3. Which type of diet will the nurse recommend for the patient while they are taking Pepto-Bismol?
a. a full-liquid diet
b. a diet high in roughage
c. a bland diet
d. a diet that avoids foods with natural pectin

4. The nurse also inquires about the patient's history of allergies to medication. Pepto-Bismol should be avoided in patients who are allergic to which drug?
a. penicillin
b. salicylates
c. naproxen sodium
d. glucocorticoids

5. The nurse recommends that the patient take Pepto-Bismol for no longer than
a. 48 h
b. 72 h
c. 96 h
d. 1 week

Case Study B

Gastrointestinal Drugs

A 30-year-old patient is taking a bus trip to New York City with a group of friends. They are anxious about the trip because they often experience motion sickness, so they consult with their physician. In the past they have experienced nausea and vomiting on long road trips and while on boats.

1. The patient’s physician suggests a medication to help prevent nausea and vomiting. Which medication will the physician most likely recommend?
  a. diphenhydramine
  b. meclizine
  c. promethazine
  d. prochlorperazine

2. After further discussion, the physician thinks that the patient would experience less motion sickness with a Transderm-Scop patch. To which area of the body is this patch applied?
  a. on the inner wrist
  b. on the upper arm
  c. behind the ear
  d. on the anterior abdomen

3. How many hours prior to the patient’s bus trip should the Transderm-Scop patch be applied to prevent motion sickness?
  a. 1 h
  b. 2 h
  c. 4 h
  d. 8 h

4. The physician discusses other options for motion sickness treatment as well. Which medication can be given by IM injection to a patient who already has motion sickness?
  a. dimenhydrinate
  b. diphenhydramine
  c. Nexium
  d. Meclizine

5. Which additional instruction regarding the Transderm-Scop patch should the physician give to the patient prior to their bus trip?
  a. The patch will be effective for 24 h.
  b. The patch may cause excitability.
  c. Do not cut the patch prior to application.
  d. The patch will work only for motion sickness caused by bus travel.

Chapter Review Quiz

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication

1. ______ Nexium
2. ______ Linzess
3. ______ Rowasa
4. ______ calcium carbonate
5. ______ Prevacid
6. ______ Transderm-Scop
7. ______ Dulcolax
8. ______ simethicone
9. ______ Imodium
10. ______ Phenergan

Condition

a. Diarrhea
b. Flatulence
c. GERD
d. heartburn
e. Nausea and vomiting
f. Constipation
g. Inflammatory bowel disease
h. Motion sickness

Choose the correct answer.

11. With antacids, which of the following applies to administration?

a. before meals
b. 2 h from other medications
c. with Tagamet
d. with milk

12. What is a frequent side effect of calcium carbonate antacids?

a. diarrhea
b. fluid retention
c. constipation
d. palpitations

13. A patient taking an antispasmodic may experience which side effect?

a. urinary retention
b. diarrhea
c. restlessness
d. excitability

14. Which of the following is the primary cause of *Clostridium difficile* infection?

a. yeast overgrowth in the colon
b. intermittent use of H_2 blocker therapy
c. eradication of native intestinal flora by antibiotics or another source
d. prolonged use of probiotics

15. When a patient complains of constipation, what is the first action that should be taken?

a. administer an osmotic laxative

b. obtain an abdominal X-ray

c. administer a bisacodyl tablet with milk

d. identify the cause of the constipation

16. An interaction of an antiemetic drug with another category of drug can result in a potentiation of a sedative effect. What is the second category of drug?

a. antiarrythmics

b. antidopaminergics

c. muscle relaxants

d. antacids

17. Which of the following medications may help patients experiencing constipation directly resulting from opioid use?

a. Movantik

b. scopalamine

c. Amitiza

d. Dulcolax

18. For patients who experience IBD that presents with severe constipation, which of the following medications can be considered?

a. Linzess

b. pantoprazole

c. Amitiza

d. bisacodyl

19. Which of the following statements is true?

a. PPIs have a longer duration of action than H_2 antagonists because they bind reversibly.

b. PPIs have a longer duration of action than H_2 antagonists because they bind irreversibly.

c. H_2 antagonists have a longer duration of action than PPIs because they bind reversibly.

d. H_2 antagonists have a longer duration of action than PPIs because they bind irreversibly.

20. Which of the following is not a use for misoprostol?

a. prevent NSAID-induced ulcers

b. terminate pregnancy

c. induce early labor in pregnant persons

d. taken in combination with ibuprofen to protect the stomach (Duexis)

Chapter 17

Respiratory System Drugs and Antihistamines

Key Terms and Concepts

Anticholinergics
Antihistamines
Antitussives
Asthma prophylaxis
Bronchodilators
Decongestants
Dry-powder inhalers (DPIs)
Expectorants
Maintenance medications
Metered-dose inhalers (MDIs)
Mucolytics
Rescue treatment
Small-volume nebulizers (SVNs)
Smoking-cessation aids
Sympathomimetics
Xanthine

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe the uses of and precautions necessary with oxygen therapy.
2. List the medications used as smoking-cessation aids and precautions for their use.
3. List the uses, side effects, and precautions or contraindications for bronchodilators and antitussives.
4. Define uses, precautions, and differences of anticholinergics, SABAs, LABAs, and combination products.
5. Explain appropriate patient education for those receiving respiratory system drugs.
6. Describe the action, uses, side effects, and contraindications of antihistamines and decongestants.
7. Describe the limitations for use and safety concerns associated with combination cough–cold–allergy products.

Respiratory Diseases and Disorders

According to the American Lung Association, lung disease is the third-leading cause of death in the United States. Respiratory diseases range from mild and self-limiting, such as the common cold, to life-threatening, such as bacterial pneumonia, pulmonary embolism, and lung cancer.

Chronic obstructive pulmonary disease (COPD) is a term that encompasses a group of progressive lung diseases—chronic bronchitis (inflammation of bronchial tubes, which leads to chronic mucus production and a wet cough) and emphysema (destruction of the tiny air sacs at the base of the lungs, diminishing the capacity and efficiency of the lungs to utilize oxygen, leading to shortness of breath and exercise intolerance). COPD is a progressive disease that worsens with time and has systemic manifestations, including muscle wasting. Cigarette smoking is the primary cause of COPD; less often, it is caused by long-term exposure to lung pollutants.

Therapeutic measures for respiratory distress include oxygen therapy, respiratory stimulants, bronchodilators, corticosteroids, mucolytics, expectorants, antitussives, and smoking cessation.

Oxygen Therapy

Oxygen is used therapeutically for hypoxia (insufficient oxygen supply to the tissues) and to decrease the workload of the heart and respiratory system, especially during distress. Some of the conditions for which oxygen therapy is indicated are heart and lung diseases such as COPD, smoke inhalation, carbon monoxide or cyanide poisoning, and some central nervous system (CNS) conditions with respiratory difficulty or failure. Oxygen may be administered by endotracheal intubation, nasal cannula, various masks, tents, or hoods.

Side effects of oxygen delivered at too high a concentration or for prolonged periods of time without proper monitoring can include:

Hypoventilation (particularly with COPD; may cause CO_2 retention and acidosis)

Confusion

Changes in the alveoli of the lungs

Blindness (in premature infants)

Cautions or contraindications apply to:

Patients with COPD (high O_2 concentrations may cause hypoventilation or apnea [cessation of breathing]).

Danger of fire when oxygen is used. Oxygen is not flammable but does support combustion. Smoking, matches, cleaning aerosols, and electrical equipment that may spark are not allowed in rooms where oxygen is in use.

Respiratory Stimulants

Respiratory stimulants include:

- Caffeine citrate in the treatment of neonatal apnea of prematurity
- Theophylline administered IV and orally to stimulate respiration in infants (as an alternative to caffeine)

Bronchodilators

Bronchodilators act by relaxing the smooth muscles of the bronchial tree, thereby relieving bronchospasm and decreasing the work of breathing. Bronchodilators are used in the symptomatic treatment of acute respiratory conditions such as asthma, as well as many forms of COPD. Classifications of bronchodilators include the sympathomimetics (adrenergics), the anticholinergics (parasympatholytics), and the xanthine derivatives.

Bronchodilator Administration

Bronchodilators can be given orally, parenterally, and by inhalation. The inhalation route of administration is preferred to minimize adverse systemic effects. Appropriate inhalation technique is essential to achieve optimal drug delivery and the therapeutic effect of aerosol inhalant medications.

Metered-dose inhalers (MDIs) remain popular because of their ease of use, efficacy, and portability. In the past, all MDIs contained chlorofluorocarbon (CFC) as the propellant. Because of its detrimental effects on the ozone layer, the use of CFC was phased out by the end of 2013. Some manufacturers have reformulated their MDIs to contain hydrofluoroalkane (HFA) as the propellant, which has not been linked to depletion of the ozone layer and is nonflammable. Other manufacturers are discontinuing production of MDIs and utilizing alternative formulations instead. MDIs are frequently used, and the use of a spacer or reservoir device can assist in optimizing drug delivery within the lungs, especially in adolescent patients (refer to Figure 17-1).

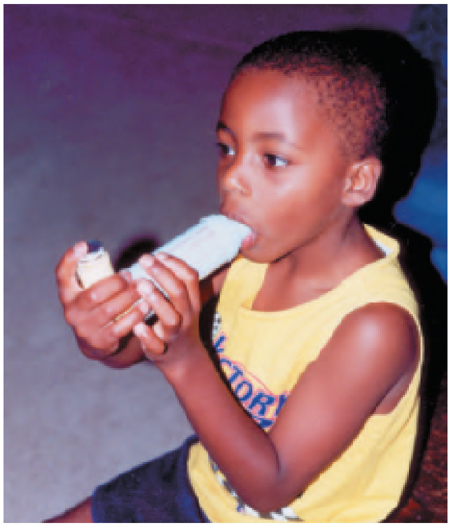


Figure 17-1 Child using a metered-dose inhaler (MDI) with a spacer and a mouthpiece.

MDIs and other inhalers need to be cleaned intermittently to avoid the build-up of medication at the mouthpiece that can inhibit drug delivery. Although it can be done more frequently, it is recommended that MDI inhalers be cleaned at least once per week. The following steps should be followed to ensure proper cleaning:

1. Remove the canister from the actuator. Do not let the canister get wet.
2. Take the cap off the mouthpiece and wash the actuator by running warm water through the top for 30 seconds.
3. Turn the actuator upside down and run warm water through the mouthpiece for 30 seconds.

4. Shake the actuator off to remove as much water as possible and allow the actuator to dry overnight.
5. Replace the canister in the actuator and shake well, spray two sprays into the air away from your face, then replace the cap on the mouthpiece.

Dry-powder inhalers (DPIs) provide medication (especially corticosteroids and long-acting beta$_2$ agonists) only under the pressure of spontaneous inspiration rather than through compression of the valve (Figure 17-2). Therefore, the patient must be able to generate sufficient inspiratory effort on their own to deliver the medication, and therefore this device should not be used in acute respiratory distress. This option is helpful for patients who are unable to coordinate inspiration with actuation of a conventional MDI.

Small-volume nebulizers (SVNs), more commonly referred to as nebulizers, create an aerosol mist of a drug solution that can then be inhaled into the lungs through a mouthpiece or a mask. The aerosol is created by either compressed air or oxygen gas, and the optimal breathing pattern is a slow, deep breath with a sustained breath hold; the aerosol should be delivered over an 8–12-min period (refer to Figure 17-3).

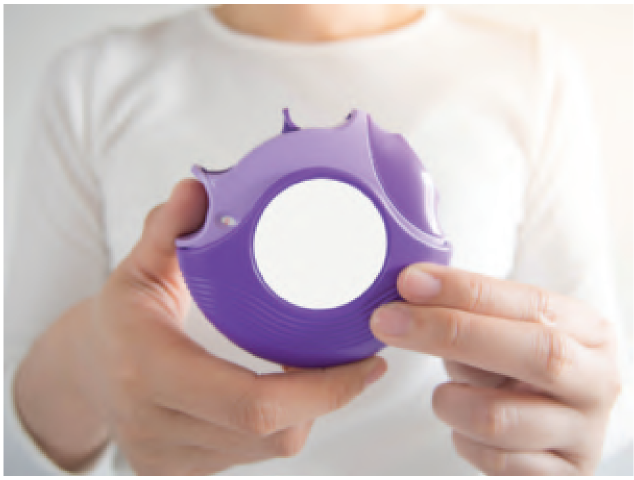

Orawan Pattarawimonchai/Shutterstock.com.

Figure 17-2 An example of a dry-powder inhaler (DPI).

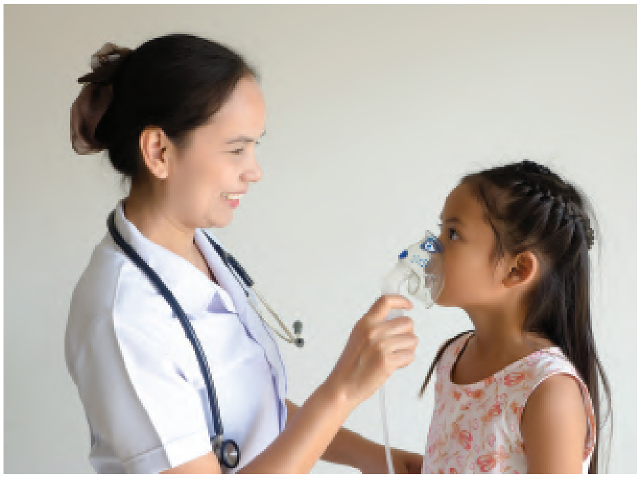

ChooChin/Shutterstock.com.

Figure 17-3 Child receiving a small-volume nebulizer (SVN) aerosol treatment with a mask.

Sympathomimetics

Sympathomimetics (adrenergics) are potent bronchodilators that increase vital capacity and decrease airway resistance. The adrenergics work on the smooth muscle in the lungs to cause relaxation. Examples include albuterol, epinephrine, and salmeterol.

An important classification system is differentiating between short-acting beta agonists (SABAs) and long-acting beta agonists (LABAs). SABAs, such as albuterol, are the drug of choice for managing acute exacerbations of asthma. LABAs, such as salmeterol, are used for prophylactic treatment. SABAs are also known as *rescue medications,* as opposed to the LABAs, which are known as **maintenance medications**.

Side effects of the adrenergics include potentiation of theophylline effects with increased risk of toxicity, especially:

Gastrointestinal (GI) (nausea, vomiting, and decreased appetite)

Cough, throat irritation, hoarseness, and sinusitis with inhaled preps

- CNS stimulation (nervousness, tremor, dizziness, and headache)
- Cardiac irregularities (tachycardia, palpitations, arrhythmias, and angina) (levalbuterol [Xopenex], an isomer of albuterol, may cause less cardiac stimulation and less incidence of certain systemic adverse reactions such as tremor and nervousness compared to albuterol; the clinical significance of these small differences is unknown)
- Hypertension
- Hyperglycemia and hypokalemia (caution with loop or thiazide diuretics)

Cautions or contraindications for the adrenergics apply to:

First administration, which should be observed by medical personnel for hypersensitivity reactions

Contacting the physician if decreased effectiveness occurs

Close monitoring, if administering oral inhaled adrenergics with other oral inhaled bronchodilators, for cardiovascular effects

Patients with cardiovascular or kidney disorders, diabetes, seizure disorders, or hyperthyroidism

Because of a prolonged onset of action, long-acting beta$_2$ agonists (such as salmeterol) should not be used to treat an acute asthma attack or bronchospasm; these are indicated only for asthma prophylaxis in combination with an asthma controller medication such as an inhaled corticosteroid. A short-acting beta$_2$ agonist (such as albuterol) should always be available for the **rescue treatment** of an acute attack. Warn patients that increasing use of rescue inhalers is a sign of deteriorating asthma control. In addition, long-acting beta$_2$ agonists have been associated with an increased risk of severe asthma exacerbations and asthma-related deaths.

Clinical Application

Rescue Inhaler Use

Rescue inhalers, which are most commonly albuterol (SABA)-based MDI inhalers, are an effective way for patients who have asthma, COPD, or other bronchospastic diseases to manage acute respiratory distress. These types of medications act very quickly, but also provide only temporary relief to patients. Overuse of SABAs can result in tachycardia, jitteriness, anxiousness, and insomnia. The recommended maximum dose for inhaled albuterol MDIs is 12 inhalations in any 24-h period. Patients should be counseled that their rescue inhaler is intended for "as-needed" use, and should not be taken if symptoms are not present. Even if a patient is not exceeding the max daily dose, it is important as a health care professional to limit rescue inhaler use, as frequent use can be a sign of poor disease state control. Ideally, patients should only require the use of the rescue inhaler two days per week or less. If patients are using the rescue relief more frequently, there is a need for maintenance therapy initiation, adjustment, or addition of new medications. Maintenance medications for respiratory diseases include inhaled corticosteroids, LABAs, oral corticosteroids, leukotriene inhibitors, and even monoclonal antibodies. The use of these medications can vary based on patient age, disease severity, and other factors. Additionally, patients can be instructed to limit activities or avoid environments that exacerbate their condition.

Anticholinergics

Anticholinergics (*parasympatholytics*), for example, Atrovent, achieve bronchodilation by decreasing the chemical that promotes bronchospasm. Anticholinergics block the parasympathetic nervous system and can cause drying of pulmonary secretions. Adequate hydration should be encouraged to avoid mucus plugging. Inhaled anticholinergics are the first-line therapy for COPD once symptoms become persistent. Refer to Table 17-1 for dosage and other product names.

Side effects of anticholinergics can include:

- ❗ Cardiac effects (changes in heart rate and palpitations)
- ❗ CNS stimulation (headache, drowsiness, dizziness, confusion, and agitation)
- ❗ Thickened secretions and mucus plugging; dry mouth and metallic taste
- Constipation and abdominal pain

Cautions: Anticholinergics are not indicated for patients with unstable cardiac status, history of heart attacks, glaucoma, drug sensitivity, or prostatic hypertrophy.

Tiotropium (Spiriva), which is structurally similar to ipratropium (Atrovent), is administered daily as a maintenance drug in a dry-powder inhaler (versus three to four times daily for ipratropium). It is more efficient than ipratropium for the maintenance treatment of COPD and may lead to a reduction in the use of sympathomimetics for rescue therapy.

Patient Education

Patients using inhaled medications should be educated on the following topics:

- Proper inhaler technique and other inhaled medication use
- Patient education for administration of various inhalation delivery systems, including MDIs, DPIs, and SVNs
- Instructions for cleaning nebulizer devices
- Instructions for taking more than one medication concurrently

Xanthines

The **xanthine** derivative theophylline, listed in Table 17-1, relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels and may possess anti-inflammatory actions. Xanthines are no longer a first-line treatment because of their modest clinical effectiveness, the need for serum monitoring, their many adverse effects, and their drug interactions.

Theophylline is generally reserved for patients with COPD who do not respond to, or cannot take, inhaled long-acting bronchodilators. When used, xanthines are usually administered as sustained-release formulations with other respiratory system drugs such as adrenergics and anticholinergics for additive effects on symptom relief and breathing functions.

Side effects of theophyllines can be mild or severe with acute toxicity, including:

- ❗ GI distress (nausea, vomiting, epigastric pain, abdominal cramps, anorexia, or diarrhea; to reduce gastric irritation, take with meals)
- ❗ CNS stimulation (nervousness, insomnia, irritability, headache, tremors, and seizures; can be fatal)
- ❗ Cardiac effects (palpitation, tachycardia, arrhythmias, *especially with rapid IV administration*)
- Urinary frequency (mild diuresis)
- ❗ Hyperglycemia

Cautions and contraindications when administering theophylline apply to:

- Sudden cessation of tobacco smoking (may result in reduced clearance of theophylline and increased serum theophylline concentrations)
- Cardiovascular, kidney, pulmonary, or liver dysfunction
- Diabetes, peptic ulcer, or glaucoma
- Children and older adults (more prone to toxicity)
- IV injection (*must be done slowly*—refer to cardiac side effects)
- Patients undergoing influenza immunization or who have influenza
- Pregnancy and lactation

Interactions occur with:

- Cimetidine, allopurinol, erythromycins, quinolones, oral contraceptives, calcium channel blockers, and beta-blockers (increase theophylline levels)
- Smoking, barbiturates, phenytoin, and rifampin (decrease theophylline effectiveness)
- Roflumilast or PDE-4 inhibitor

Refer to Table 17-1 for a summary of the sympathomimetic, anticholinergic, and xanthine bronchodilators.

Note

Roflumilast (Daliresp) is a drug that acts as a selective, long-acting inhibitor of the enzyme PDE-4, a contributor to inflammation, and therefore has anti-inflammatory effects. Roflumilast is an *orally* administered drug for the prevention of inflammatory conditions of the lungs in chronic obstructive pulmonary disease but currently has many dose-limiting side effects, including nausea, diarrhea, and headache; it must be used with at least one long-acting bronchodilator.

Table 17-1 Bronchodilators

Generic Name	Trade Name	Dosage
Sympathomimetics		
Short-Acting Beta$_2$ Agonists (Rescue Medications)		
albuterol sulfate	Proair HFA Ventolin HFA	MDI, 1–2 puffs (90–180 mcg) q4–6h
	Accuneb (Nebulizer solution) ProAir RespiClick ProAir DigiHaler	Inhal sol 2.5 mg q4–6h Oral sol, tabs 2–4 mg q6–8h MDI, 1–2 puffs (90–180 mcg) q4–6h
	Vospire ER	Tabs ER 4–8 mg q12h
levalbuterol	Xopenex	Inhal sol 0.63–1.25 mg tid (q6–8h); max 3.75 mg per day
	Xopenex HFA	MDI, 1–2 inhal (45–90 mcg) q4–6h
Long-Acting Beta$_2$ Agonists* (Maintenance Medications)		
arformoterol	Brovana	Inhal sol 50 mcg q12h (for COPD only)
formoterol	Foradil Aerolizer	Powder for inhal, 12 mcg (contents of 1 cap) q12h
	Perforomist	Inhal sol 20 mcg bid
salmeterol	Serevent Diskus	Powder for inhal, 1 puff (50 mcg per blister) q12h
olodaterol	Striverdi	MDI, 2 puffs (2.5 mcg) qd

Generic Name	Trade Name	Dosage
Sympathomimetics		
Others		
epinephrine	Adrenalin	IM/subcu 1:1,000 sol 0.3–0.5 mL; watch dose carefully!
racepinephrine	Asthmanefrin (OTC)	1–3 inhalations, max of 3 q3h
Anticholinergics		
Short-Acting		
ipratropium bromide	Atrovent HFA	MDI, 1–2 puffs (17–34 mcg) three to four times per day (max 12 sprays per day)
	Atrovent	Inhal soln, 1 unit dose (500 mcg/2.5 mL NS) three to four times per day
		Nasal sol 0.03%–0.06%, 2 sprays each nostril three to four times per day (up to 4 days for cold, 3 weeks for rhinitis)
ipratropium/albuterol (combination of anticholinergic and sympathomimetic)	Combivent Respimat	Inhal soln, 1 puff four times per day (max 6 puffs per day)
	DuoNeb	Neb sol 1 vial (3 mL) four times per day (max 6 doses per day)
Long-Acting		
tiotropium	Spiriva HandiHaler	Powder for oral inhal, 18 mcg daily (for COPD only)
aclidinium	Tudorza Pressair	1 puff (400 mcg) bid
umeclidinium	Incruse Ellipta	1 puff (62.5 mcg) daily
Combination with LABA		
umeclidinium vilanterol	Anoro Ellipta	1 actuation daily (62.5 mg/25 mcg)
aclidinium and formoterol	Duaklir	1 inhalation bid
tiotropium and olodaterol	Stiolto Respimat	2 puffs daily
Combination with LABA and Corticosteroid		
fluticasone, umeclidinium, vilanterol	Trelegy Ellipta	1 actuation daily (100 mg/62.5 mg/25 mcg)—COPD 1 actuation daily (100 mg/62.5 mg/25 mcg) or (200 mg/62.5 mg/25 mcg)—asthma
Xanthines		
theophylline	RTU infusion in D_5W	Dosage based on response and drug levels
	Elixophyllin	Elixir, 80 mg/15 mL
	Theo-24	Caps ER, 100–400 mg daily

*__Note:__ Because of the delayed onset of action, long-acting beta_2 agonists should never be used to treat an acute attack and should be used in combination with an inhaled corticosteroid. This is a representative list. Other products are available.

Patient Education

Patients taking bronchodilators (e.g., adrenergics, anticholinergics, or the xanthines) should be instructed regarding:

- Following the written directions on the package very carefully regarding dosage and administration because of the danger of serious side effects
- The differences between rescue medications and long-term controllers
- Proper technique for inhaler use; capsules used with DPIs must not be swallowed
- Use of spacers for patients who have difficulty using MDIs
- Watching closely for cardiac irregularities or CNS stimulation (e.g., nervousness, tremor, dizziness, confusion, and headache), and reporting these symptoms to the physician immediately
- Other side effects possible with adrenergics and xanthines, for example, gastric distress, insomnia, or hyperglycemia
- Drinking adequate fluids to prevent mucus plugging, especially with anticholinergics
- The importance of quitting smoking and avoiding secondhand smoke, fumes, or pollution
- Asthma guidelines stating that OTC bronchodilators are *not recommended* because the temporary relief provided may delay the patient from seeking medical care
- Avoiding any new medications, including OTC drugs, without consulting the physician first, because of the danger of serious complications; many interactions are possible
- Avoiding changing brands of medicine without consulting the physician or pharmacist

Corticosteroids

Synthetic corticosteroids are used to relieve inflammation, reduce swelling, decrease bronchial hyper-responsiveness to triggers, and suppress symptoms in acute and chronic reactive airway disease (asthma and some COPDs). Corticosteroids should be administered systemically (oral and injectable forms) for short-term "bursts" during exacerbations and occasionally at the beginning of treatment until symptoms are controlled. Comparatively, inhaled corticosteroids are used chronically for prophylaxis, and are not used as acute bronchospasm treatment.

Inhaled

Inhaled corticosteroids (SVN aerosol, DPI, and MDI) are considered a preferred drug therapy in long-term prophylactic management of persistent asthma of various severities. Regular long-term treatment reduces exacerbations, improves control of symptoms and lung function, and reduces hospital admissions and deaths from asthma. Inhaled corticosteroids with long-acting beta agonists are also used on a regular, long-term, scheduled basis in patients with COPD to improve symptoms and quality of life. Inhaled corticosteroids have fewer systemic side effects than oral or injectable administration. They are often used in combination with LABAs. Patients should be counseled to rinse their mouth out with water after use and to not swallow medication. Failure to follow these instructions could result in oral thrush or irritation of the esophageal passage.

Intranasal

Nasal corticosteroids are increasingly considered first-line therapy for most *noninfectious* types of rhinitis and reduce congestion, edema, and inflammation. They should be started before symptoms occur and taken regularly throughout the period of exposure. Aerosol corticosteroid preparations seem to be more irritating (burning, sneezing) to the nasal mucosa. Aqueous preparations may drip into the throat, resulting in reduced deposition of drug in the nasal mucosa.

Side effects of inhaled corticosteroids:

❗ Throat irritation and dry mouth
Hoarseness
❗ Oral fungal infections (patient should be encouraged to rinse mouth with mouthwash or water after administration)
❗ Increased susceptibility to pneumonia

Cautions or contraindications with corticosteroids apply to:

Viral, bacterial, or fungal infections
Hypertension or congestive heart failure
Diabetes
Hypothyroidism or cirrhosis
Renal failure

Refer to Table 17-2 for a summary of corticosteroids.

Table 17-2 Corticosteroids

Generic Name	Trade Name	Dosage
Corticosteroids (Inhaled and Intranasal)		
beclomethasone	QVAR HFA	MDI, 1–2 puffs (40 or 80 mcg per puff) bid
	Beconase AQ	Spray (42 mcg) 1–2 inhal each nostril daily, bid
budesonide	Pulmicort Flexhaler	Powder for inhal, 180–360 mcg bid
	Pulmicort Respules	Neb susp, 0.25–1 mg daily or bid; indicated for children ≥ 8 years old
	Rhinocort Aqua	Aerosol 1–4 inhal each nostril daily (32 mcg per spray)
with glycopyrrolate and formoterol	Breztri Aerosphere	Two inhalations BID
with formoterol	Symbicort	MDI, 2 puffs (80/4.5, 160/4.5) bid
fluticasone furoate	Arnuity Ellipta	MDI, 1 puff daily (100–200 mcg)
with vilanterol	Breo Ellipta	MDI, 1 puff daily (100–200 mcg/25 mcg)
fluticasone propionate	Flovent HFA	MDI, 2–4 puffs bid (88–880 mcg)
	ArmonAir Digihaler)	DPI, 55-232 mcg/dose
	Flonase	Spray (50 mcg) 1 inhal each nostril bid or 2 inhal daily
with salmeterol	Advair Diskus (100/50, 250/50, 500/50)	Powder for inhal, 1 inhal q12h

(*Continued*)

Table 17-2 Corticosteroids (*Continued*)

Generic Name	Trade Name	Dosage
	Advair HFA (45/21, 115/21, 230/21)	MDI, 2 puffs q12h
	Wixela (DPI)	One inhalation BID
	Airduo	One inhalation BID
ciclesonide	Alvesco HFA	MDI, 1 puff BID (80-160 mcg)
mometasone	Asmanex Twisthaler	Powder for inhal, 220 mcg bid or 440 mcg qPM
with formoterol	Dulera	Two inhalations BID
	Nasonex	Spray 2 inhal each nostril daily (50 mcg per spray)
triamcinolone	Nasacort AQ (Rx)	Inhaler, 1–2 inhal each nostril daily (55 mcg/inhal)
	Nasacort Allergy 24HR (OTC)	Inhaler, once daily (age 2 and older), not to exceed 2 months a year; dosing varies per age group

Note: This is a representative list. Other products are available. Breo Ellipta comes with two foil blister strips; each dose contains one blister from each strip (one contains fluticasone furoate, and the other contains vilanterol).

Asthma Prophylaxis

Leukotriene Inhibitors

Zafirlukast (Accolate) and montelukast (Singulair) are oral leukotriene receptor antagonists for **asthma prophylaxis**, prevention of exercise-induced bronchoconstriction, and treatment of chronic asthma. Leukotriene receptor antagonists primarily help to control the inflammatory process of asthma caused by leukotriene production, thus helping to prevent asthma symptoms and acute attacks. They can be used as monotherapy or as add-on therapy in patients whose persistent mild to moderate asthma is inadequately controlled with inhaled corticosteroids. Montelukast can be used in children as young as 2 years old and has fewer drug interactions compared to zafirlukast.

Side effects of Singulair include:

❗ Headache
❗ Dizziness
Nausea or dyspepsia
Pain
Fatigue
Respiratory infections and fever
Behavior or mood changes, sleep disturbances, and suicidal ideation

Cautions or contraindications apply to:

Hepatotoxicity (zafirlukast)
Pregnancy or lactation
Treatment of acute episodes of asthma (these are *not* rescue medications)

Drug interactions occur with:

Aspirin (increased levels of zafirlukast)
Erythromycin and theophylline (decreased levels of zafirlukast)
Warfarin and zafirlukast (increased prothrombin time)
Phenobarbital and rifampin (decreased levels of montelukast)

Mast Cell Stabilizers

The rupture or degranulation of mast cells and the subsequent spilling of their chemical mediator contents cause an inflammatory response that can lead to asthma. Stabilizing the mast cell membrane has anti-inflammatory actions that modify the release of mediators from mast cells and eosinophils.

A prophylactic for asthma, cromolyn was one of the first classified mast cell stabilizers. Cromolyn has no value in the treatment of acute attacks of asthma. It has also been used in the prevention of exercise-induced bronchospasm. Cromolyn is available as a solution for inhalation or a nasal solution (to treat seasonal allergic rhinitis) for use in adults and children as young as 2 years old. To be effective, the manufacturer's directions must be followed carefully.

Side effects of cromolyn can include:

❗ Throat irritation, cough, and bronchospasm
❗ Nose burning, stinging, and sneezing (with nasal solution)

Caution applies to:

Those with cardiovascular disorders

Eosinophilic Asthma Agents (IL-5 monoclonal antibodies)

Many patients with asthma can be treated effectively with the proper use of maintenance medications, but those with a less common type of asthma called eosinophilic asthma may not. Eosinophilic Asthma is characterized by increased eosinophil blood counts. Recently, the new IL-5 receptor antagonists benralizumab (Fasenra), reslizumab (Cinqair) and mepolizumab (Nucala) were approved by the FDA for maintenance use in severe eosinophilic asthma. These medications are not to be used to treat acute symptoms.

Side effects of IL-5 monoclonal antibodies can include:

❗ Injection site reactions
❗ Headache

Caution applies to:

Those who have previously had an allergic reaction to this product
Those who are exposed to opportunistic infections

Refer to Table 17-3 for a summary of asthma prophylaxis.

Table 17-3 Asthma Prophylaxis Agents

Generic Name	Trade Name	Dosage
Asthma Prophylaxis and Treatment of Chronic Asthma		
Mast Cell Stabilizers		
cromolyn sodium	NasalCrom (OTC)	Inhal sol, 20 mg per treatment four times per day Inhaler, 1 spray each nostril three to four times per day
Leukotriene Inhibitors		
montelukast	Singulair	Tabs 10 mg qPM Chew tabs, 4–5 mg qPM
zafirlukast	Accolate	Tabs 10–20 mg bid on empty stomach
zileuton	Zyflo Zyflo CR	600 mg qid 1,200 mg bid with meals
IL-5 monoclonal antibodies		
benralizumab	Fasenra	30 mg SQ q4-8w
reslizumab	Cinqair	3 mg/kg IV q4w
mepolizumab	Nucala	100-300 mg SQ q4w

Note: This is a representative list. Other products are available.

Patient Education

Patients treated with inhaled corticosteroids or the asthma prophylaxis agents should be instructed regarding:

- The fact that these agents are *not* effective for acute exacerbations of asthma or immediate symptom relief
- Proper technique for inhaler use
- Side effects to expect, such as throat irritation, dry mouth, and cough (rinse mouth and gargle to minimize), and with products administered nasally; for example, nose burning, stinging, or sneezing are possible with cromolyn
- Complications of inhaled corticosteroids without proper precautions, for example, oral fungal infections (patient should be encouraged to rinse mouth with mouthwash or water after treatment and to always rinse and air dry equipment after use)
- Administering bronchodilator before the corticosteroid when the two inhaled medications are ordered at the same time
- Reporting side effects to the physician, especially respiratory distress
- The importance of not smoking

Mucolytics and Expectorants

Mucolytics, such as acetylcysteine, decrease the hypersecretion of and liquefy pulmonary secretions. Thick secretions can be a problem in patients with obstructive lung disease, but there is little evidence that *inhaled* acetylcysteine is more effective than adequate hydration for thinning or increasing the clearance of secretions.

Cautions or contraindications for mucolytics apply to:

Asthma or a history of bronchospasm (IV administration or inhalation may result in acute bronchospasm or anaphylaxis)

Respiratory insufficiency, inadequate cough mechanism, or gag reflex depression (liquefied pulmonary secretions can occlude the airway if the patient is unable to adequately clear the secretions)

Expectorants, such as guaifenesin (the only agent approved for use as an expectorant), increase secretions, reduce viscosity, and help to expel sputum but, like mucolytics, offer little clinical benefit for patients with obstructive lung disease. Adequate fluid intake is important to maintain normal fluid volume, but excessive fluid intake is of no value.

Guaifenesin is commonly combined in cough syrups for the symptomatic management of productive ("wet") coughs associated with upper respiratory tract infections, bronchitis, pharyngitis, influenza, measles, or coughs provoked by sinusitis, but evidence of benefit is lacking. It is also commonly used in combination with a cough suppressant, dextromethorphan, to reduce the incidence of dry cough, but still loosen mucus in the respiratory tract to allow for productive cough.

Expectorants should not be used for self-medication for persistent or chronic coughs such as those associated with smoking or COPD. A persistent cough may be indicative of a serious condition. If the cough persists for more than a week, is recurrent, or is accompanied by a fever, a physician should be consulted.

Side effects of the expectorants are infrequent, usually not serious at recommended doses, and can include:

❗ Nausea and vomiting, and diarrhea

Drowsiness, dizziness, and headache

Cautions or contraindications for expectorants apply to:

Persistent or chronic cough

Some asthmatics (prone to bronchospasm)

Cardiovascular disease and hypertension, diabetes, glaucoma, hyperthyroidism, and prostatic hypertrophy, especially with combination products

Pregnancy or lactation

Refer to Table 17-4 for a summary of the mucolytics and expectorants.

Table 17-4 Mucolytics and Expectorants

Generic Name	Trade Name	Dosage
Mucolytic		
acetylcysteine	(Mucomyst)[a]	Neb soln, 3–5 mL 20% sol (diluted) or 6–10 mL 10% sol (undiluted) three to four times per day; give short-acting bronchodilator 10–15 min prior to dose

(*Continued*)

Table 17-4 Mucolytics and Expectorants (*Continued*)

Generic Name	Trade Name	Dosage
Expectorant		
guaifenesin	Mucinex	ER tabs 600–1,200 mg, daily bid; do not crush
	Robitussin	Sol 2–4 tsp q4h as needed

Note: Guaifenesin is frequently combined with other drugs, for example, analgesics, antihistamines, decongestants, and antitussives in OTC and prescription respiratory combination products.

[a] This brand name is no longer marketed, but the name is still commonly used.

Antitussives

Antitussives are medications intended to prevent coughing in patients who are not actively generating a productive cough. Coughing, a reflex mechanism, helps eliminate secretions from the respiratory tract. A dry, nonproductive cough can cause fatigue; insomnia; and, in some cases, pain to the patient (e.g., pleurisy and fractured ribs). Most antitussives produce cough suppression by acting centrally on the cough center located in the brainstem. Cough suppressants are divided into narcotic preparations, such as codeine and hydrocodone, and non-narcotic preparations, such as dextromethorphan.

Codeine, a *narcotic antitussive,* is widely used as a cough suppressant owing to its reduced incidence of side effects (respiratory depressant action and bronchial constriction) at antitussive doses as compared to morphine. In some states, codeine is available behind the pharmacy counter as an OTC cough medication. Hydrocodone, another narcotic cough suppressant, has slightly greater antitussive activity compared to codeine but is more sedating. With the recent change from Drug Enforcement Agency (DEA) Schedule III to DEA Schedule II, hydrocodone is prescribed less frequently as an antitussive, but liquid formulations are still available for severe coughing.

Clinical Application

FDA Black Box Warnings

Black box warnings are required by the FDA for certain medications that have the potential for serious safety risks. Usually black box warnings communicate potential rare but dangerous side effects (injury and death), and they may also serve to communicate important instructions for safe use of the drug.

A black box warning was added to the drug label of codeine-containing products about the risk of codeine used to *manage pain* in children after a tonsillectomy and/or adenoidectomy. Some children have died after being given codeine in amounts that were within the recommended dose range. Codeine is converted to morphine in the liver by an enzyme. Some people are ultra-rapid metabolizers who are more likely to have higher-than-normal amounts of morphine in their blood after taking codeine. High levels of morphine can result in breathing difficulty, which may be fatal. Although this warning applies to codeine as a pain reliever, it bears consideration when codeine is used as an antitussive. Genetic testing can be utilized to identify if a child is an ultra-rapid, extensive, intermediate, or poor metabolizer of codeine.

Non-narcotic antitussives (e.g., dextromethorphan) are used more frequently because they do not depress respirations, do not cause dependence, and have few side effects at recommended doses. They are considered to have a similar antitussive effect as codeine at the same dose. Dextromethorphan should not be used in patients under the age of 4 years (caution in age less than 6 years) because of the cough center in the brain not being fully developed. Benzonatate (Tessalon), chemically related to the local anesthetic tetracaine, suppresses cough peripherally by anesthetizing receptors in the alveoli of the lungs, the bronchi, and the pleura; it also acts centrally like the other antitussives. Diphenhydramine (Benadryl), a first-generation antihistamine, is also used as a cough suppressant and is described in detail later in this chapter.

Side effects of antitussives can include:

❗ Respiratory depression (large doses or excessive use)—only narcotic antitussives

Constipation—only narcotic antitussives

Urinary retention—only narcotic antitussives

❗ Sedation and dizziness—only narcotic antitussives

Nausea and vomiting

Cautions or contraindications for antitussives apply to:

Patients prone to addiction

Asthma; COPD

Other CNS depressants

Caution for antitussives with children can include:

Some CNS side effects, behavioral disturbances, and respiratory depression reported, especially with large doses

Ester-type anesthetic (e.g., tetracaine) hypersensitivity with *benzonatate*

Interactions with dextromethorphan can include:

Triptans used for migraine headache

Monoamine oxidase inhibitors (MAOIs), resulting in serotonin syndrome (applies to benzonatate as well)

The SSRIs fluoxetine and paroxetine (reduce dextromethorphan dose)

Memantine (Namenda)

The American College of Chest Physicians practice guidelines do not recommend the use of cough suppressants for coughs associated with upper respiratory infection (URI) because of their limited efficacy. It is recommended that patients experiencing a cough associated with the common cold or postnasal drip associated with a URI use a first-generation antihistamine and a decongestant to treat the cough.

Refer to Table 17-5 for a summary of the antitussives.

Table 17-5 Antitussives

Generic Name	Trade Name	Dosage	Comments
Narcotic			
codeine with guaifenesin	Cheratussin AC	Syrup 10–20 mg q4–6h	Antitussive dose is lower than that required for analgesia; any cough medicine containing a controlled substance is not for extended use; can develop physical dependence and tolerance; watch for side effects DEA schedule V
codeine with promethazine	(Phenergan)[a] with codeine		
hydrocodone with homatropine[b]	Hydromet	Syrup or tabs 5 mg q4–6 h	DEA schedule II
with chlorpheniramine	Tussionex	ER Susp, 5 mL q12h	DEA schedule II
Non-narcotic			
benzonatate	Tessalon[a]	Caps 100–200 mg tid	Related to tetracaine; swallow caps whole RX only
dextromethorphan	Delsym	ER susp, 10 mL (60 mg) q12h	Note interactions OTC
with guaifenesin	Robitussin DM	Sol 10–20 mg q4h or Sol 30 mg q6–8h	OTC
	Mucinex DM	Tab (200–400/10–20 mg) 1 to 2 taken bid	Extended release; do not crush or chew OTC
diphenhydramine	Benadryl	Caps, tabs, liquid 25 mg q4–6h Caps, tabs 50 mg	Antihistamine with anticholinergic effects, especially drying 25 mg—OTC 50 mg—Rx only

[a] This brand name is no longer marketed, but the name is still commonly used.

[b] An anticholinergic agent is added in subtherapeutic amounts to some hydrocodone products to discourage deliberate overdosage.

Patient Education

Patients taking antitussives should be instructed regarding:

- Reading and carefully following the directions on the product label
- Starting with a low dose of antitussives and increasing the dose only if cough suppression does not occur
- Avoiding use with alcohol and other CNS depressants
- Taking care in operating machinery because of sedative effects

Antihistamines

Antihistamines competitively antagonize the histamine$_1$-receptor sites. Through this action, the antihistamines combat the increased capillary permeability and edema, inflammation, and itch caused by sudden histamine release. Antihistamines are used to treat the symptoms of allergies (e.g., rhinitis, conjunctivitis, and rash). Please refer to Figure 17-4. However, when antihistamines are used to reduce nasal secretions in the common cold, the consequent thickening of bronchial secretions may result in further airway obstruction, especially in those with COPD and asthma. H_1-blockers are grouped into two categories: first-generation agents and second-generation agents.

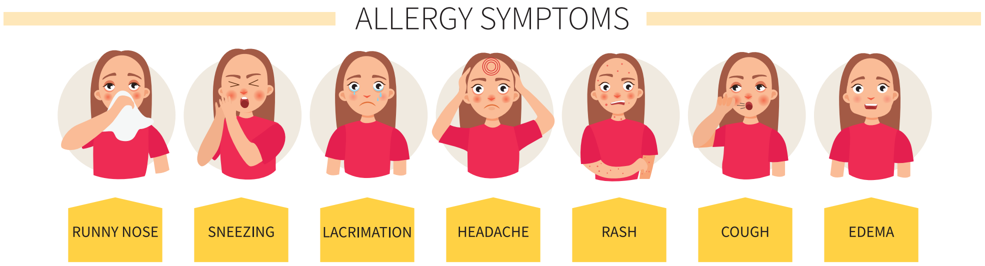


Figure 17-4 Antihistamines and nasal corticosteroids (discussed previously in this chapter) decrease the inflammatory response that causes seasonal allergies.

Igdeeva Alena/Shutterstock.com.

First Generation

These antihistamines, such as diphenhydramine (Benadryl), were the first group of medications available to treat symptoms of allergies. Diphenhydramine is also approved as an antitussive, nighttime sleep aid, and antiemetic. It is also used as an adjunctive treatment of anaphylactic reactions after the acute symptoms (e.g., laryngeal edema and shock) have been controlled with epinephrine and corticosteroids or used as monotherapy for minor local allergic reactions or irritation from things like insect stings and bites. Some antihistamines are used in the symptomatic treatment of vertigo associated with pathology of the middle ear or in the prevention and treatment of motion sickness. First-generation antihistamines tend to have more side effects than second-generation antihistamines because they are not selective for the histamine$_1$-receptors.

Learning Hint

When comparing side effects of selective and nonselective medications, an easy way to remember which will have a higher number and/or more severe side effects is to think of them like firearms. A shotgun fires many small pellets in a wide radius from its target line, and although it hits its intended target, there is high potential for an unintended target to be hit. This is what a nonselective medication is like—although it will bind to its intended receptor, it may also bind to other unintended receptors, causing side effects. On the other hand, selective medications are more like a rifle. When it fires, it sends a single bullet on a straight path directly toward its target, limiting unintended collateral damage. Selective medications tend to bind only to a certain receptor (or bind primarily to one receptor), which limits unintended side effects.

Side effects of the first-generation antihistamines are primarily anticholinergic in action and include:

- ❗ Drying of secretions, especially of the eyes, ears, nose, and throat
- ❗ Sedation, dizziness, tachycardia, and hypotension, especially in older adults
- Muscular weakness and decreased coordination; cognitive impairment
- Urinary retention and constipation
- Visual disorders
- ❗ Paradoxical excitement, insomnia, and tremors, especially in children
- GI effects—nausea, vomiting, and anorexia
- Nasal irritation, epistaxis, and bitter taste with nasal spray

Cautions or contraindications for first-generation antihistamines apply to:

- COPD and asthma
- Persons operating machinery or driving a car
- Older adult patients (extended half-life with sedation)
- Closed-angle glaucoma
- Cardiovascular disorders
- Benign prostatic hyperplasia (BPH)
- Children under the age of 6 years
- Pregnancy and lactation
- Seizure disorders

Interactions of first-generation antihistamines may occur with:

- Potentiation of CNS depression with tranquilizers, analgesics, hypnotics, alcohol, and muscle relaxants

Patient Education

Patients taking first-generation antihistamines should be instructed regarding:

- Avoiding frequent or prolonged use of antihistamines (may cause increased bronchial or nasal congestion and dry cough)
- *Not* using antihistamines to sedate children
- Not self-medicating (check with the physician first) in those with COPD or cardiovascular disorders, BPH, older adults, and children
- Taking care in driving or operating machinery because of the sedative effect
- Not mixing with alcohol or any other CNS depressant drugs

Second Generation

The *second-generation antihistamines* include fexofenadine (Allegra), cetirizine (Zyrtec), levocetirizine (Xyzal), and loratadine (Claritin). These drugs are *selective* (have greater specificity for) histamine$_1$-receptor antagonists and have fewer CNS effects, for example, less sedation, and fewer anticholinergic effects compared to the first-generation antihistamines. Although these agents cause little or no sedation, it is important to note that the incidence of sedation is not zero. They are used to provide symptomatic relief of seasonal allergic rhinitis, for example, hay fever. The second-generation antihistamines are not effective in the treatment of cough.

Side effects of second-generation antihistamines, usually mild, can include:

Headache, dizziness, fatigue, and drowsiness (especially cetirizine)
Dry mouth and pharyngitis

Cautions or contraindications for second-generation antihistamines apply to:

Asthma
Renal and hepatic impairment
Hydroxyzine (Vistaril) allergy with Zyrtec
Driving or operating machinery
Pregnancy or lactation
Children less than 2 years of age

Patient Education

Patients taking second-generation antihistamines should be instructed regarding:

Avoiding any other drug, including OTC, without consulting the physician first
Reporting symptoms such as fainting, dizziness, or palpitations to the physician immediately
Using caution with driving or operating machinery until you know how these drugs affect you

Decongestants

Several adrenergic drugs, for example, phenylephrine (Neo-Synephrine) and pseudoephedrine (Sudafed), act as **decongestants**. These drugs constrict blood vessels in the respiratory tract, resulting in the shrinkage of swollen mucous membranes (because of colds or allergies) and helping to open nasal airway passages. Given orally, they are less effective than topical decongestants and have the potential for systemic side effects, especially increasing blood pressure. However, these drugs, both oral and nasal, should be used only on a short-term basis because rebound congestion may occur within a few days.

Decongestants are frequently combined with antihistamines, analgesics, caffeine, and/or antitussives. Many of these products are available OTC, and by combining several drugs, the possibility of adverse side effects is increased, especially without adequate medical supervision.

The Combat Methamphetamine Epidemic Act of 2005 (which took effect in 2006) banned OTC sales of ingredients commonly used to make methamphetamine. Psuedoephedrine (PSE), a popular and effective oral nasal decongestant, was the primary target of the act. PSE can now be stored and sold only in limited quantities under special conditions (behind the counter) by pharmacies in an attempt to limit its sale in large quantities. Purchasers are limited to 3.6 g (15 days of the max daily dose) of PSE per day and 9 g per month. Pharmacies are limited in the amount that can be sold per day as well.

Newer formulations of PSE have been marketed as an abuse deterrent and have now become the primary single-source PSE product that pharmacies choose to stock. Nexafed and Zephrex-D, when taken correctly, supply the intended amount of PSE to the patient, but both formulations make it very difficult to extract PSE by crushing, dissolving, and so on. This makes it much more difficult to abuse.

Side effects of decongestants can include:

- ❗ Anxiety, nervousness, insomnia, tremor, and seizures
- ❗ Palpitations, tachycardia, hypertension, headache, and cerebral hemorrhage
- Reduced cardiac output and reduced urine output
- Burning, stinging, sneezing, and dryness with nasal preparations

Cautions or contraindications for decongestants apply to:

- Cardiovascular disorders
- Hyperthyroid or diabetes
- Older adults—especially those with glaucoma or BPH
- Pregnancy or lactation

Interactions may occur with:

- Potentiation of adverse side effects with other adrenergics, ergot, tricyclics, MAOIs

Refer to Table 17-6 for a summary of the antihistamines and decongestants.

Note

Saline nasal spray (e.g., Ocean) is a safe, effective treatment option for nasal congestion.

Patient Education

Patients taking decongestants should be instructed regarding:

- Using decongestants for only a few days (3 days for nasal; 7 days for oral) to avoid rebound congestion
- Avoiding when cardiac or thyroid conditions or diabetes are present
- Discontinuing with side effects such as nervousness, tremor, palpitations, or headache
- Avoiding combining with any other medications without consulting the physician

Table 17-6 Antihistamines and Decongestants

Generic Name	Trade Name	Dosage
First-Generation Antihistamines		
azelastine (Rx)	Astelin, Astepro	1–2 sprays per nostril bid
chlorpheniramine	Chlor-Trimeton, Aller-Chlor	Liquid 2 mg/5 mL q4–6h Tabs 4 mg q4–6h ER caps, tabs 8 mg tid–12 mg bid
clemastine (Rx/OTC)	Tavist Allergy	Syrup, tabs 1.34–2.68 mg bid–tid

Generic Name	Trade Name	Dosage
diphenydramine (Rx/OTC)	Diphenhist	Liquid 25–50 mg q4–6h
	Benadryl Allergy	Tabs 25–50 mg q4–6h
	Benadryl	IM or IV 10–50 mg q4–6h
Second-Generation Antihistamines		
cetirizine (OTC)	Zyrtec	Syrup, tabs 5–10 mg per day
desloratadine (Rx)	Clarinex	Syrup, tabs 5 mg daily
Fexofenadine (OTC)	Allegra	Susp, tabs 30–60 mg bid, 180 mg per day
levocetirizine (Rx)	Xyzal	Soln, tabs 2.5–5 mg per day
loratadine (OTC)	Claritin, Alavert	Syrup, tabs 10 mg daily
Decongestants		
oxymetazoline	Afrin	Sol 1–2 of 0.05% sprays, drops q12h
phenylephrine	Neo-Synephrine	Sol 0.125%–1%, 2–3 drops/sprays q4h;
	Sudafed PE	Tabs 10 mg q4–6h
In combination with various cough and cold preparations (OTC)	Alka-Seltzer Plus Tylenol Multi-Symptom Vicks DayQuil	10 mg in all combination products
pseudoephedrine	Sudafed	Sol or tabs 30–60 mg q4–6h Tabs ER 120 mg q12h or 240 mg q24h
	Nexafed Zephrex-D	30 mg abuse-deterrent formulation
In Combination with Second-Generation Antihistamines		
cetirizine (OTC) fexofenadine (OTC) loratadine (OTC)	Zyrtec D Allegra D Claritin D	ER formulations containing 120 mg of PSE for 12-h tablets and 240 mg for 24-h tablets Taken daily or bid

Rx = available by prescription only; Rx/OTC = availability depends on product labeling.

Note: This is a representative list. Many prescription and OTC drugs have combinations of antihistamines, decongestants, and/or antitussives. Many second-generation antihistamines are available in combination products with a decongestant (pseudoephedrine). These products can be identified by being labeled with a capital D (e.g., Claritin D).

Safety of Cough–Cold–Allergy Products

Many prescription and OTC cough and cold formulations are available that combine several drugs—for example, antitussives with expectorants, antihistamines, and decongestants—to treat two or more simultaneous symptoms. Combination formulations should be used only if the corresponding symptom is present and each individual component is available in the proper strength and dosing interval a patient may need. Patients should be cautioned to seek advice from a health care professional familiar with each ingredient. The health care professional should thoroughly assess each patient's use of similar products (both OTC and Rx) to avoid duplication of therapy and the potential for inadvertent overdose. Some ingredients are contraindicated in certain medical conditions, as detailed earlier.

In 2011, the FDA required removal of many *prescription* cough, cold, and allergy products from the market that were never approved by the FDA. Many of the unapproved drug products covered by the 2011 action contained the same ingredients as the *OTC* cough and cold preparations that were the subject of a 2008 public health advisory. Whereas the FDA's Nonprescription Drugs and the Pediatric Advisory Committee found there was no proof that these medications eased cold symptoms in children, there were reports that they caused serious adverse effects, overdose, and even deaths. At that time, many manufacturers voluntarily removed from the market cough and cold products labeled for use in children under 2 years old, and some products were relabeled to state that they were not for use in children under 4 years old.

In addition to product labeling changes, new child-resistant packaging and measuring devices for the products were introduced. With the changing status of cough and cold medications, a website (https://www.fda.gov/drugs/understanding-over-counter-medicines/tips-parents-about-safe-use-over-counter-otc-medicine) is available for parents and caregivers seeking information on the use of these medicines in children.

Patient Education

Patients taking respiratory system drugs should be instructed regarding:

- Use of appropriate non-drug measures for the patient's particular symptoms
- Care in taking medications only as prescribed and required; do not give children medicine labeled only for adults
- Use and safety concerns of combination products
- Avoiding combining respiratory system drugs with other prescription or OTC drugs or alcohol, which could potentiate CNS stimulation or depression, resulting in serious adverse side effects
- Choosing OTC cough and cold medications with child-resistant safety caps; using only measuring devices that come with the product or those made for measuring the medicine
- Avoiding self-medication when cardiac, thyroid, or CNS conditions are present
- Benefits from desensitization therapy and air-conditioned environmental control for patients with allergic conditions
- Avoiding air pollution (e.g., smoke-filled rooms)
- Exercises (e.g., swimming) that increase lung capacity and help reduce the necessity for the medication
- Importance of receiving (and safety of) inactivated influenza vaccinations in adults and children with asthma, which can reduce serious illness, complications, and mortality
- Proper use of inhalers when prescribed
- Not crushing, chewing, or breaking extended-release preparations; swallow whole

Smoking-Cessation Aids

Cigarette smoking is the leading cause of preventable disease and death in the United States. Most smokers fail to quit on their first try, and after experiencing how difficult quitting is, many will never try again. All **smoking-cessation aids** have been shown to help twice as many smokers quit as quitting “cold turkey” (abrupt and complete withdrawal from an addictive substance) when used properly and in conjunction with nonpharmacologic therapies (behavioral modification and social support system).

Nicotine Replacement Therapy

Nicotine replacement products (Table 17-7), including Nicorette gum, Commit lozenges, the Nicoderm CQ patch (Figure 17-5), and the Nicotrol inhaler and nasal spray, help to lessen withdrawal symptoms by slowly lowering the level of nicotine in the body. They let the person who smokes focus on breaking the social habits of nicotine and participating in a behavior modification program for smoking cessation without battling the withdrawal symptoms at the same time. The most effective method is for patients to use one long-acting nicotine replacement method (e.g., patch) and one “rescue” nicotine replacement method (e.g., gum) for breakthrough cravings.

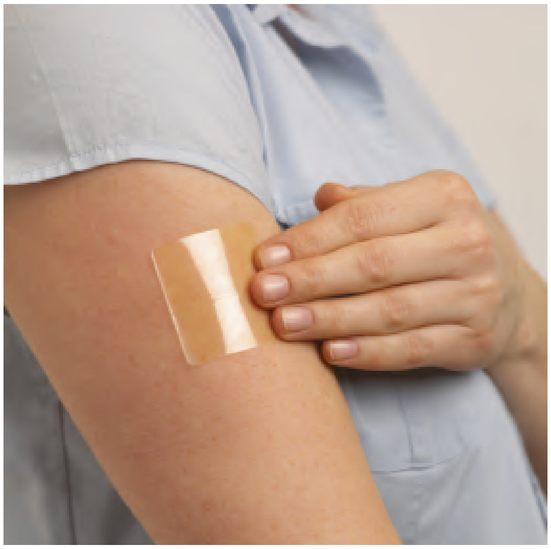
Electronic cigarettes (or e-cigarettes) are battery-powered devices that heat liquid nicotine into an inhaled vapor (“vaping”), which simulates tobacco smoking. E-cigarettes should *theoretically* have fewer toxic effects (because of fewer toxic chemicals) than traditional cigarettes, but concrete evidence is lacking. Although e-cigarettes have not yet been linked to any serious health issues, they have been in widespread use for such a short period of time that there is no basis for determining if there are long-term risks.

Side effects of nicotine replacement products (which could also be related to nicotine withdrawal symptoms) can include:

- ! Mechanical problems with chewing gum, especially if the patient has dentures
- ! Cardiac irritability
- ! Chewing too quickly (may cause lightheadedness, nausea, heartburn, vomiting, and throat and mouth irritation)
- Skin reaction at the application site

Cautions or contraindications for nicotine replacement products apply to:

Dental problems that might be exacerbated by chewing gum
Drug abuse and/or overdependence



Daniel Heighton/Shutterstock.com.

Figure 17-5 Nicotine patches can be applied for up to 12 h, then taken off overnight.

Overdosage—studies have shown that combination therapy (nicotine patch plus one other form of nicotine replacement) is more effective if the user is unable to quit using a single agent, but there is little safety data on this, and combination therapy may increase the risk of nicotine overdose

Pregnancy and lactation

Unstable cardiovascular disease

Patients *should be warned not to smoke*

Proper disposal of used nicotine patches and other nicotine-containing formulations to avoid accidental ingestion by children and pets

Bupropion

Bupropion is an oral antidepressant drug (Wellbutrin) that is also prescribed as an aid to smoking cessation (marketed as Zyban) and has been associated with decreases in cravings for cigarettes and lessening of nicotine withdrawal. Zyban is also indicated for use in combination with nicotine patches for treating the symptoms of nicotine withdrawal.

Varenicline

Varenicline (Chantix) is a prescription-only partial nicotine receptor agonist–antagonist given orally and indicated for adults as an aid in smoking cessation. It alleviates the symptoms of nicotine craving and withdrawal through its agonist activity while inhibiting the effects of repeated nicotine exposure by its antagonist activity, thus eliminating the pleasurable feelings associated with smoking. Mild to moderate nausea and vomiting, sleep disturbance, and abnormal dreams are the most common side effects, with nausea and vomiting occurring in nearly one-third of patients (it should be taken after a meal with fluids). To date, no clinically significant drug interactions have been identified.

There have been reports of serious neuropsychiatric symptoms, such as changes in behavior, agitation, depressed mood, and suicidal ideation and behavior associated with varenicline. There is some controversy as to whether these were caused by complications owing to nicotine withdrawal or by the drug itself. The safety and efficacy of varenicline in patients with serious psychiatric disorders such as schizophrenia, bipolar disorder, and major depression have not been established. Patients and caregivers should be aware of the need to monitor for these symptoms and report them immediately to the physician.

Refer to Table 17-7 for a summary of smoking cessation aids.

Table 17-7 Smoking-Cessation Aids

Generic Name	Trade Name	Dosage
nicotine	Nicorette	1 piece of gum (2 or 4 mg) whenever urge to smoke, up to 24 pieces per day for up to 12 weeks
	Commit	1 lozenge (2 or 4 mg) after waking up; no more than 5 loz in 6 h/20 loz per day for up to 12 weeks

Generic Name	Trade Name	Dosage
	Nicoderm CQ	First dose: 21 mg patch per day, 6 weeks
		Second dose: 14 mg patch per day, 2 weeks
		Third dose: 7 mg patch per day, 2 weeks
	Nicotrol NS (Rx)	1 spray each nostril one to two times per hour; max 10 sprays/h or 80 sprays per day for up to 12 weeks; taper doses over 4 to 6 weeks
	Nicotrol inhaler (Rx)	24–64 mg (6–16 cartridges) daily up to 12 weeks and then gradual reduction in dose lasting 6–12 weeks
bupropion	Zyban (Rx)	Tabs, SR 150 mg daily for 3 days and then 150 mg bid for 7–12 weeks for up to 6 months maintenance; start 1 to 2 weeks before quit date
varenicline	Chantix (Rx)	Tabs, 1 mg bid, following a 1-week titration for 12 weeks with additional 12-week course if needed

Rx = available by prescription only.

Case Study A

Respiratory Medications

A patient has had asthma for 4 years. During their annual physical, they explain that they use their rescue inhaler more than once a day every day of the week.

1. The physician decides to start the patient on a new medication, montelukast. The physician explains that this medication works by

a. controlling the inflammatory process caused by leukotrienes

b. producing an antihistamine effect

c. suppressing the cough associated with asthma

d. liquefying pulmonary secretions and thus promoting increased air flow

2. When starting montelukast, the patient should be prepared for which potential side effect?

a. flushing of face and hands

b. dry cough

c. headache

d. tinnitus

3. One advantage of montelukast over other asthma medications is that it

a. can be used as monotherapy or as an add-on therapy

b. has no drug interactions

c. can be taken during pregnancy and breastfeeding

d. can be used as a rescue drug

4. Montelukast belongs to which category of drugs?

a. asthma rescue

b. asthma curative

c. asthma prophylaxis

d. asthma acute exacerbation

5. What is a side effect of montelukast that should promptly be reported to a physician?

a. throat irritation

b. suicidal ideation

c. fatigue

d. double vision

Case Study B

Respiratory Medications

During a visit to an urgent care clinic, a patient is diagnosed with a severe sinus infection. The nurse practitioner prescribes an antibiotic and an oral decongestant.

1. A decongestant's primary action in opening nasal passages is to
a. reduce nasal irritation
b. anesthetize receptors in nasal passages
c. thicken bronchial secretions
d. constrict blood vessels in the respiratory tract

2. A potential systemic side effect of a decongestant is
a. bradycardia
b. hypertension
c. sedation
d. hypotension

3. Prior to prescribing the decongestant, the nurse practitioner carefully reviews the patient's chart because decongestants are contraindicated in individuals with
a. pregnancy
b. depression
c. asthma
d. multiple sclerosis

4. To avoid the potential complications of rebound congestion, the patient is cautioned to take the oral decongestant for no more than
a. 3 days
b. 7 days
c. 10 days
d. 30 days

5. When the patient goes to the pharmacy, how will they be able to purchase the decongestant pseudoephedrine?
a. OTC
b. by prescription only
c. from the pharmacist behind the counter
d. only in combination with an antihistamine

Chapter Review Quiz

Match the medication in the first column with the condition that it is used to treat in the second column. Conditions may be used more than once.

Medication

1. _______ Allegra
2. _______ Commit
3. _______ guaifenesin
4. _______ Xopenex
5. _______ Spiriva
6. _______ Tessalon
7. _______ cromolyn sodium
8. _______ Accolate
9. _______ Zyban
10. _______ Nexafed

Condition

a. Bronchospasm (anticholinergic)
b. Chronic asthma
c. Asthma (adrenergic)
d. Asthma (prophylactic)
e. Allergies
f. Smoking cessation
g. Bronchitis (unproductive cough)
h. Congestion

Choose the correct answer.

11. Which of the following is not a consideration or concern when using oxygen therapy?

a. hypoventilation
b. danger of fire
c. blindness (in premature infants)
d. can only be administered via nasal cannula

12. What is the first-line therapy for noninfectious rhinitis?

a. nasal corticosteroids
b. oral corticosteroids
c. aqueous preparations
d. aerosol preparations

13. A potential side effect of inhaled corticosteroids is

a. staining of teeth
b. throat irritation
c. canker sores
d. excessive salivation

14. When educating a patient prior to initiating an inhaled corticosteroid, which instruction is most important?

a. Expect an increased susceptibility to influenza.
b. Use only half of one dose if experiencing dry mouth.
c. Exhale immediately after inhaling the dose.
d. Rinse your mouth with water or mouthwash after administration.

15. What is an appropriate instruction for patients taking second-generation antihistamines?

a. Take OTC medications as needed—no restrictions.
b. Take laxatives in conjunction with the antihistamine to avoid constipation.
c. Use caution when driving or operating machinery.
d. Expect palpitations that will resolve over time.

16. How should bronchodilators be administered in conjunction with corticosteroids?

a. administer the bronchodilator immediately before the corticosteroid
b. administer the corticosteroid immediately before the bronchodilator
c. administer the medications 4 h apart
d. administer the medications 2 h apart

17. A mucolytic is contraindicated in patients

a. with pharyngitis

b. with swollen lymph nodes

c. taking oral steroids

d. with a depressed gag reflex

18. What cough medication is frequently used for cough because it does not depress respirations?

a. dextromethorphan

b. codeine

c. guaifenesin

d. mometasone

19. What side effect is most likely to occur with large doses of antitussives?

a. urinary retention

b. constipation

c. respiratory depression

d. nausea

20. Antitussives frequently contain controlled substances that are not available OTC. Which of the following medicines does not contain a controlled substance and is available OTC?

a. Hyromet

b. Delsym

c. Tussionex

d. Cheratussin AC

21. Cough and cold medications containing antihistamines are appropriate only when the cause of the cough is

a. asthma

b. allergic rhinitis

c. emphysema

d. smoking

22. Nicorette would be an appropriate treatment for an individual with which condition?

a. arrhythmia

b. dentures

c. pregnancy

d. a smoker with COPD

23. Individuals taking first-generation antihistamines can expect anticholinergic side effects such as

a. hypertension

b. drying of secretions

c. tearing of the eyes

d. bradycardia

24. If a patient currently using nicotine patches to quit smoking asks if they can use anything for breakthrough cravings, which of the following would be the appropriate response?

a. Yes, you can use nicotine gum, lozenges, or an inhaler for cravings.

b. Yes there is, but only if you are having cravings more than 10 times per day.

c. For safety reasons, you should never use two nicotine products concurrently.

d. No there isn't, because although you can use two nicotine products at the same time, it would be a waste of money to use both.

25. Which of the following can be used to treat an acute bronchospasm?

a. SABAs

b. LABAs

c. inhaled corticosteroids

d. cholinergics

Chapter 18

Eye and Ear Medications

Key Terms and Concepts

Antiglaucoma drugs
Anti-infective
Anti-inflammatory
Beta-adrenergic blockers
Carbonic anhydrase inhibitors
Cycloplegic
Intraocular pressure (IOP)
Miotics
Mydriatics
Otic
Otitis media
Rho kinase inhibitors

Objectives

Upon completion of this chapter, the learner should be able to:

1. Demonstrate the administration technique for instillation of ophthalmic and otic medications.
2. Describe the five categories of ophthalmic medication.
3. Identify side effects, precautions and contraindications, and interactions for each category of ophthalmic medication.
4. Explain appropriate patient education necessary for each category of eye and ear medications.
5. Describe common uses for otic medications.

According to the National Eye Institute, the most common eye diseases in Americans 40 years and older are age-related macular degeneration, glaucoma, cataracts, and diabetic retinopathy. Conjunctivitis, or inflammation of the conjunctiva (commonly referred to as pink eye or red eye), is one of the most frequent causes of patients of any age seeking help for an eye-related ailment. Allergens, irritants, mechanical abrasions, bacteria, and viruses all can cause conjunctivitis. Medications for the eye discussed in this chapter can be classified into five categories: anti-infectives, anti-inflammatory agents, antiglaucoma agents, mydriatics (pupil dilation), and local anesthetics.

Anti-Infectives

Many **anti-infective** ophthalmic topical ointments and solutions are available for the treatment of superficial infections of the eye caused by organisms. In general, whereas ointments are preferable to drops for use in children, patients with poor adherence, and nighttime administration, drops are preferred in adults and daytime administration because ointments will cause blurring of vision for 20 min after instillation. To reduce the development of drug-resistant bacteria and maintain the effectiveness of antibacterial drugs, it is important to determine the causative organism when possible.

Ophthalmic antibiotic preparations (singly and/or in combination) include macrolides, bacitracin, fluoroquinolones, sulfonamides, bacitracin–polymixin, and trimethoprim–polymyxin. Aminoglycosides are used less frequently owing to their toxicity to the corneal epithelium. Antiviral ophthalmic drops like ganciclovir are used when a viral infection is suspected. When treating infections, if there is no improvement in 2 to 3 days, physicians should suspect microbial resistance, inappropriate choice of drug, or incorrect diagnosis. In these cases, the antibiotic can be switched to a different class, or the patient may have to return for a follow-up appointment.

In general, topical therapy is used for 7–10 days. Prolonged use may result in the overgrowth of nonsusceptible organisms, including fungi. Always check the latest literature regarding resistant organisms and check the patient's history regarding allergies.

Patient Education

Patients being treated with anti-infective ophthalmic preparations should be instructed regarding:

- Using only as directed and checking dosage and frequency
- Carefully instilling into the lower conjunctival sac to avoid contamination of the tip of the dropper or ointment tube (Figure 18-1)
- Possible hypersensitivity reactions in patients with allergies of any kind
- Discontinuing the medication and reporting immediately to a physician any signs of sensitivity (e.g., burning and itching)
- Careful handwashing to prevent the spread of infection to the other eye or other persons
- Not using eye makeup or not wearing contact lenses while treating eye infections
- Replacing eye makeup and contacts due to possible contamination by the causative organism
- Never reusing an anti-infective ophthalmic drop from a previous infection
- When using more than one ophthalmic product at the same time, spacing them at least 5 min apart (to ensure maximum absorption) and administering the more viscous preparation (i.e., ointment, suspension) *last*

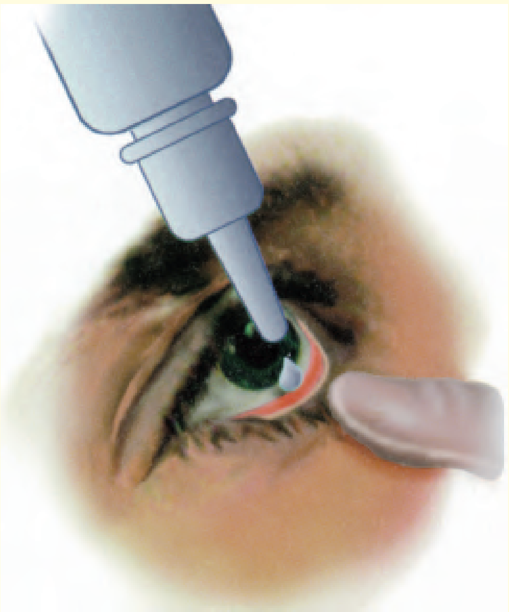


Figure 18-1 Instilling eye medication. Gently pull the lower lid down and have the patient focus eyes upward. Ophthalmic solution is dropped inside the lower lid.

Side effects of anti-infectives can include hypersensitivity reactions such as conjunctivitis, irritation, local burning, stinging, blurred vision, rash, and urticaria in persons with a history of allergy.

Cautions or contraindications for anti-infectives apply to:

Anyone allergic to the drug
Viral and fungal diseases of the ocular structure

Interactions may occur with prolonged use of corticosteroids, which can result in secondary ocular infections caused by suppression of immune response.

Other antiviral ophthalmic preparations used topically in the treatment of herpes simplex, keratitis (inflammation of the cornea), or conjunctivitis include trifluridine (Viroptic) ophthalmic solution. The dose is one drop to the lower conjunctival sac of the infected eye up to 9 times daily at 2-h intervals while awake (maximum 9 drops per eye per day or 21 days per episode).

Anti-inflammatory Agents

Anti-inflammatory ophthalmic agents are used to relieve inflammation of the eye or conjunctiva in allergic reactions, burns, irritation from foreign substances, or postoperatively.

Corticosteroids

Various topical forms of the corticosteroids are also useful in the *acute* stages of eye injury to prevent scarring, for severe symptoms, or when the condition is unresponsive to other medications. However, corticosteroids should not be used for extended periods because of the danger of masking the symptoms of infection or slowing the healing process. In general, ophthalmic corticosteroids should be prescribed cautiously because they may cause sight-threatening complications when used inappropriately. Application of ophthalmic corticosteroids topically does not generally cause systemic effects. However, systemic absorption can be minimized by applying gentle pressure on the inner canthus of the eye following instillation of corticosteroid ophthalmic drops or ointment (Figure 18-2).

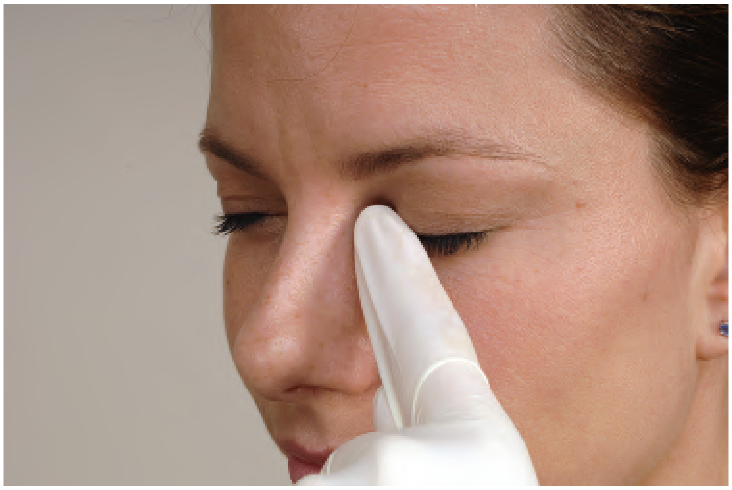


Figure 18-2 Apply gentle pressure on the inner canthus following administration of ophthalmic medications. Systemic absorption is thus minimized with medications such as corticosteroids, miotics, and mydriatics.

Side effects of corticosteroids can include:

- Increased intraocular pressure (IOP) depends on the drug, dose, frequency, and length of treatment; less likely with fluorometholone)
- Reduced resistance to bacteria, viruses, or fungi
- Delayed healing of corneal wounds, thinning of cornea, and corneal ulceration
- Stinging, burning, or ocular pain
- Increased risk of developing cataracts

Cautions or contraindications with corticosteroids apply to:

Acute bacterial, viral, or fungal infections
Primary open-angle glaucoma
Pregnancy
Prolonged use

Ophthalmic corticosteroids are also available in combination with other antibiotics (i.e., Tobradex—tobramycin and dexamethasone; Blephamide—sulfacetamide and prednisolone). They are used to treat steroid-responsive inflammatory ocular conditions in which a corticosteroid is indicated and bacterial infection or risk of infection exists.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drug (NSAIDs) such as flurbiprofen (Ocufen) and ketorolac (Acular) ophthalmic drops are used to treat postoperative inflammation following cataract surgery. NSAIDs are not generally first-line agents for other eye conditions with inflammation, but are an alternative to corticosteroids if a contraindication exists.

Caution applies to those who may be allergic to aspirin and other NSAIDs. Topical NSAIDs are relatively safe, with few local or systemic side effects. Ketorolac may sting or burn during application, but this may be alleviated by refrigerating the solution before use.

Ophthalmic Immunologic Agent

Topical cyclosporine (Restasis) increases tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation. It is an immunosuppressive agent for organ transplant rejection prophylaxis when administered systemically. However, the risk of systemic toxicity is minimal when given topically. Topical cyclosporine has demonstrated long-term efficacy and safety in the treatment of dry eye disease (other treatments are not recommended for long-term use). Lifitegrast (Xiidra) is a newer medication that is in a class of medications called lymphocyte function-associated antigen-1 (LFA-1) antagonist. Lifitegrast is also considered an immunologic agent and works by reducing the swelling in the eye tissues. It is indicated for the treatment of the signs and symptoms of dry eye disease.

Side effects of topical cyclosporine and other immunologic ophthalmic agents, which are mild and transient, include ocular burning, itching, stinging, pain, and blurred vision.

Cautions or contraindications apply to patients with active ocular infections; topical cyclosporine has not been studied in patients with a history of herpes keratitis.

Antihistamines or Decongestants

Ophthalmic administration of antihistamines blocks histamine receptors in the conjunctiva, relieving ocular pruritis–associated allergic conjunctivitis. Ophthalmic administration of decongestants causes vasoconstriction of blood vessels, thereby providing relief from minor eye irritation and redness. These two classes of drugs are also used in combination (i.e., Naphcon-A, Visine-A). The most common use for ophthalmic antihistamines is for seasonal allergies that precipitate symptoms such as redness, itchiness, or other irritation.

Many of these products contain the preservative benzalkonium chloride, which can accumulate in contact lenses, causing irritation. Manufacturers recommend that these products be used for no more than 72 h. Patients should stop using a product and visit a physician if they experience eye pain, changes in vision, continued redness or irritation of the eye, or any persistent condition.

Ophthalmic Lubricants

Ocular lubricants such as artificial tear solutions provide a barrier function at the level of the conjunctival mucosa. They help to dilute and flush various allergens and inflammatory mediators that may be present on the ocular surface. Artificial tear products that contain preservatives may cause allergic reactions and should be stopped immediately. There are many ophthalmic lubricants available over the counter (Systane, Refresh, and Genteal are representative examples). Ophthalmic lubricants are considered to be very safe and can be used as often as needed.

Refer to Table 18-1 for a summary of anti-inflammatory ophthalmic drugs.

Table 18-1 Anti-inflammatory Ophthalmic Drugs

Generic Name	Trade Name	Dosage
Corticosteroids		
fluorometholone	FML	Oint, susp; varies with condition
prednisolone	Omnipred, Pred Forte	Sol, susp; varies with condition
	Many combinations with antibiotics	Oint, sol, susp; varies with condition
dexamethasone	Maxidex	Sol, susp, implant; varies with condition
	Many combinations with antibiotics	Oint, sol, susp; varies with condition
loteprednol	Lotemax	Sol, susp; varies with condition
Difluprednate	Durezol	Emulsion (does not need to be shaken); varies with condition
Nonsteroidal Anti-inflammatory Drugs		
flurbiprofen	Ocufen	Sol; varies with condition
ketorolac	Acular, Acular LS	Sol; varies with condition
bromfenac sodium	Prolensa	Sol; varies with condition
diclofenac	Voltaren	Sol; varies with condition
Immunologic agent		
cyclosporine	Restasis	Emulsion 0.05%; 1 drop q12h
lifitegras	Xiidra	Sol 5%; 1 drop q12h

Note: Check percent and dose ordered *carefully*! Follow directions. Do not use for longer than prescribed.

This is a representative sample; many other products are available.

Patient Education

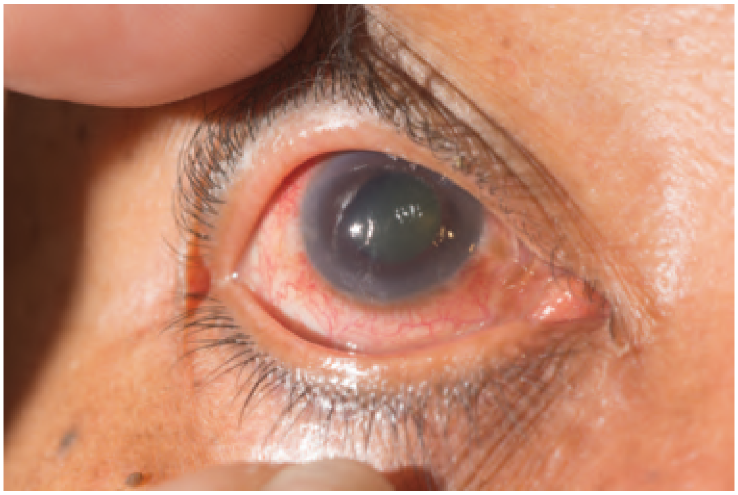
Patients being treated with anti-inflammatory ophthalmic drugs should be instructed regarding:

- Not rubbing their eyes, which can worsen the condition
- Following directions carefully regarding time and amount
- Lowered resistance to infection—do not use long term
- Administration (i.e., applying pressure on tear duct at inner corner to reduce systemic absorption) (refer to Figure 18-2)
- Not wearing contact lenses if eyes are red
- Removing lenses prior to using the product; contacts may be reinserted for most products if eyes are not red
- Not using leftover drug for new eye inflammations—discard the drug when no longer needed

Antiglaucoma Agents

Glaucoma is a group of sight-threatening diseases of the eye in which there is increased **intraocular pressure (IOP)** due to obstruction of the outflow of aqueous humor. Please refer to Figure 18-3. This causes deterioration of and damage to the optic nerve (which carries images on the retina to the brain), resulting in vision loss. According to the Centers for Disease Control and Prevention (CDC), approximately 3 million Americans have glaucoma, and it is the second leading cause of blindness worldwide. Nearly half of those with glaucoma are unaware they have the disease. There are two main types of glaucoma:

1. ***Acute (angle-closure) glaucoma.*** Characterized by a sudden onset of pain, blurred vision, and a dilated pupil, this condition is considered a *medical emergency.* Although uncommon, if left untreated, blindness can result in a few hours or days. Treatment consists of miotics (e.g., pilocarpine), osmotic agents (e.g., mannitol), carbonic anhydrase inhibitors (e.g., acetazolamide), and surgery to open a pathway for the release of aqueous humor.



ARZTSAMUI/Shutterstock.com.

Figure 18-3 Glaucoma is caused by excessive intraocular pressure, which can make the eye appear irritated and watery.

2. ***Chronic (open-angle) glaucoma.*** Much more common and often bilateral, this condition develops slowly over a period of years with few symptoms except a gradual loss of peripheral vision and possibly blurred vision. Halos around lights and central blindness are late manifestations. Treatment consists of miotics, carbonic anhydrase inhibitors, and a local beta-adrenergic blocker, such as timolol (Timoptic) eye drops.

The first step in glaucoma therapy is early diagnosis via screening and ensuring the patient abstains from medications that may exacerbate glaucoma (i.e., potent corticosteroids, anticholinergics, and antihistamines). **Antiglaucoma drugs**, given to lower intraocular pressure, can be divided into five main categories based on their mode of action:

1. ***Carbonic anhydrase inhibitors,*** for example, dorzolamide (Trusopt). They act by decreasing the formation of aqueous humor and have a diuretic effect.
2. ***Miotics,*** for example, pilocarpine. They act by increasing the aqueous humor outflow.
3. **Beta-adrenergic blockers,** for example, timolol. They act by decreasing the rate of aqueous humor production.
4. ***Alpha-agonists,*** for example, brimonidine (Alphagan-P). They decrease the production of aqueous humor and increase outflow.
5. ***Prostaglandin analogs,*** for example, latanoprost (Xalatan). They act by increasing aqueous outflow. A newer class of medication called **Rho kinase inhibitors** also act to increase aqueous outflow, but through a different mechanism of action than that of prostaglandin analogs.

Note

There is no cure for glaucoma, and any vision damage that has already occurred cannot be reversed. It is very important to continue treatment for a lifetime once diagnosed and to have regular eye exams to prevent further vision damage. This is especially important for patients who are diabetic and predisposed to developing glaucoma.

Currently, the beta-adrenergic blockers and prostaglandin analogs are the most frequently used topical medications. Drugs in different categories are sometimes given concomitantly. Combination products are available as well, for example, timolol combined with dorzolamide (Cosopt) or with brimonidine (Combigan).

Carbonic Anhydrase Inhibitors

Carbonic anhydrase inhibitors (CAIs) such as acetazolamide reduce the formation of hydrogen and bicarbonate ions, which have a diuretic effect and reduce the production of aqueous humor. Oral acetazolamide (Diamox Sequels) has largely been replaced by topical preparations, which have fewer side effects, but is occasionally used in the adjunctive treatment of open-angle glaucoma or short-term preoperatively (IV or regular-release tabs) to reduce IOP in angle-closure glaucoma and is given with miotics.

Side effects of *oral and IV* CAIs, infrequent and usually dose related, can include:

Thirst, taste alteration; frequent urination

❗ Drowsiness, fatigue, confusion, and seizures

❗ Hepatic and renal disorders (can lead to kidney stones)

❗ Photosensitivity (avoid excessive sunlight exposure)

Cautions or contraindications with CAIs apply to:

- Chronic obstructive pulmonary disease (COPD)
- Diabetes
- Electrolyte, hematological, hepatic, pulmonary, and renal disorders
- Sulfonamide hypersensitivity
- Pregnancy and lactation

Interactions with CAIs are frequent because of increasing or decreasing excretion of other drugs and can include:

- Decreased effects of lithium and oral antidiabetics
- Increased effects of quinidine, amphetamines, and other diuretics
- Hypokalemia with thiazides and corticosteroids

Dorzolamide (Trusopt) is a CAI that is applied *topically* to treat open-angle glaucoma. It is used as an adjunct to beta-blockers and is available as a combination product with timolol (Cosopt).

Side effects of dorzolamide can include:

- ❗ Burning or stinging and blurred vision
- Bitter taste

Caution applies to:

- Those with sulfonamide hypersensitivity
- Concurrent ophthalmic and oral CAIs

Patient Education

Patients being treated with CAIs should be instructed regarding:

- Reporting side effects and response to the physician for appropriate dosage regulation
- Importance of follow-up with the physician

Miotics, Direct-Acting

Miotics are medications that cause the pupil to contract. Miotics reduce IOP by increasing the aqueous humor outflow. They act by contracting the ciliary muscle; this mechanism also leads to blurred vision. Miotics (e.g., pilocarpine) are used in the treatment of open-angle glaucoma (considered third-line therapy due to side effects) or in the short-term treatment of angle-closure glaucoma before surgery.

Pilocarpine is also used after ophthalmic examinations in patients with glaucoma to *constrict the pupil* and counteract the *mydriatic* (pupil-dilating) effects of other agents. Miotics are usually administered with acetazolamide and/or timolol. Because of its increased duration of effect and less frequent administration, pilocarpine hydrochloride gel (Pilopine HS) may provide some advantages over ophthalmic solutions, especially for long-term use with patients who are noncompliant.

Pilocarpine has cholinergic action and side effects.

Side effects of pilocarpine, usually dose related, can include:

- ❗ Blurred vision and myopia
- ❗ Twitching, stinging, and burning
- ❗ Ocular pain and headache
- ❗ Photophobia and poor vision in dim light
- Cataracts and retinal detachment (due to ciliary muscle spasm)

Systemic effects with frequent or prolonged use or high doses of pilocarpine, especially in children, can include:

- ❗ Increased lacrimation, salivation, and sweating
- ❗ Hypotension and bradycardia
- ❗ Bronchospasm

Cautions or contraindications with pilocarpine apply to:

- Angle-closure glaucoma *with acute inflammation*
- History of retinal detachment or retinal degeneration
- Acute inflammatory processes
- Soft contact lenses in place
- Corneal abrasion

Interactions of pilocarpine may occur with:

- Topical atropine, which reduces effectiveness

Patient Education

Patients being treated with miotics should be instructed regarding:

- Following directions carefully regarding time and amount
- Administering by closing tear duct after instillation (refer to Figure 18-2)
- Reporting side effects to the physician for possible dosage adjustment
- Administering at bedtime to reduce side effects
- Not driving at night

Beta-Adrenergic Blockers

Timolol (Timoptic) is a *nonselective* beta-adrenergic blocker that is used topically to lower IOP in open-angle glaucoma by decreasing the rate of aqueous humor production.

Side effects of beta-adrenergic blockers are infrequent and transient but may include:

- Ocular irritation, tearing, conjunctivitis, or diplopia
- Transient blurred vision with the gel formulation

- ❗ Aggravation of *preexisting* cardiovascular or pulmonary disorders, which may cause bradycardia, hypotension, dizziness, and bronchospasm

Cautions or contraindications with beta-adrenergic blockers apply to:

- Bradycardia, heart failure, and heart block
- Patients receiving oral beta-blocker drugs
- Asthma and chronic obstructive pulmonary disease (COPD)—betaxolol (Betoptic-S) can be used *with caution* in patients with bronchospastic pulmonary disease because it does not affect the pulmonary receptors
- Pregnancy and lactation
- Children
- Diabetes and hyperthyroidism
- Closed-angle glaucoma

Interactions of beta-blockers may occur with:

- Other antiglaucoma drugs to help lower IOP
- Oral beta-blockers to increase chances of hypotension, bradycardia, and heart block

Patient Education

Patients being treated with beta-adrenergic blockers should be instructed regarding:

- Administering by closing tear duct after instillation to reduce systemic effects (refer to Figure 18-2); do not exceed the recommended number of drops
- Caution in patients with cardiac or pulmonary disorders or who are taking oral beta-blockers
- Importance of regular eye examinations
- Continuous use of medications for glaucoma; *do not discontinue abruptly*
- When administering more than one ophthalmic medication, allowing a time interval (at least 5 min) between medications; ophthalmic solutions should always be used before gels and suspensions to optimize the absorption of each medication

Alpha Agonists

Brimonidine (Alphagan-P) is a selective alpha$_2$ agonist that decreases the formation and increases the outflow of aqueous humor. It does this without causing mydriasis and with minimal effects on cardiovascular or pulmonary hemodynamics. Brimonidine is an alternative for those for whom topical beta-blocker therapy is contraindicated.

Side effects of alpha agonists can include:

- Conjunctival redness, itchiness, stinging
- Dizziness, drowsiness, dry mouth, and headache
- The potential to enhance the CNS depressant effects of ethanol, opiate agonists, anxiolytics, sedatives, and hypnotics

Patient Education

Patients being treated with alpha agonists should be instructed regarding reporting side effects to the physician immediately.

Because drugs in this class may cause fatigue or drowsiness in some patients, those who engage in hazardous activities should be cautioned of the potential for a decrease in mental alertness.

Prostaglandin Analogs

Regarded as first-line agents, latanoprost (Xalatan), travoprost (Travatan Z), and others are prostaglandin analogs that cause the greatest reduction in IOP by increasing the outflow of aqueous humor. They may be used concomitantly with other topical ophthalmic drugs to lower IOP (administer the drugs at least 5 min apart).

Side effects of prostaglandin analogs include:

Blurred vision, burning, macular edema, and stinging

Slow, gradual change in the color of the iris (resultant color change may be permanent)

Change in the length, thickness, and pigmentation of eyelashes (Latisse, a form of bimatoprost, is approved for the treatment of hypotrichosis, or inadequate eyelashes)

Cautions or contraindications with prostaglandin analogs apply to:

Active intraocular inflammation (may worsen condition)

Contact lens wearers

Hepatic and renal diseases

Pregnancy, lactation, and use in children

Drug interaction of prostaglandin analogs occurs with eye drops containing the preservative thimerosal (precipitation occurs). If such drugs are used, administer them with an interval of at least 5 min between applications. There are no other clinically significant drug interactions.

More frequent administration of prostaglandin analogs than the dosage indicated in Table 18-2 may actually decrease their IOP lowering effect. Refrigerate unopened bottle of Xalatan; once opened, the container may be stored at room temperature for 6 weeks. Travatan does not require refrigeration.

Patient Education

Patients being treated with prostaglandin analogs should be instructed regarding:

Possibility of iris color change (increase of the brown pigment)

Contacting the physician immediately if ocular reactions develop

Prostaglandin analogs contain a preservative that may be absorbed by contact lenses; remove lenses prior to administration of the drug and wait 15 min before reinserting

Rho kinase inhibitors

A newer class of medications, Rho kinase inhibitors act to lower eye pressure by relaxing the trabecular meshwork and connection passageway, called Schlemm's canal. This canal drains the aqueous humor from the anterior chamber of the eye into the veins draining the eyeball. Netarsudil (Rhopressa) is the only approved drug in this class and it is generally administered as a single drop in the affected eye in the evening.

Side effects of Rho kinase inhibitors include:

Eye redness
Pain or stinging
Blurred vision

Cautions or contraindications with Rho kinase inhibitors apply to:

Contact lens wearers

Refer to Table 18-2 for a summary of antiglaucoma agents.

Table 18-2 Antiglaucoma Agents

Generic Name	Trade Name	Dosage
Carbonic Anhydrase Inhibitors		
acetazolamide	(Diamox)[a]	Tab, IV, 125–250 mg two to four times per day (max 1 g per day)
	Diamox Sequels	ER cap 500 mg PO bid (max 1 g per day)
brinzolamide	Azopt	Ophthalmic sol 1% 1 drop q8h
dorzolamide	Trusopt	Ophthalmic sol 1 drop tid
Miotics[b], Direct-Acting		
pilocarpine HCl	Isopto Carpine	Ophthalmic sol 1%, 2%, 4%[c], 1 drop up to four times per day
pilocarpine gel	Pilopine HS	Ophthalmic gel 4%[c] at bedtime
Beta-adrenergic blockers		
timolol	Timoptic	Ophthalmic sol 0.25–0.5%, 1 drop bid
	Timoptic-XE	Ophthalmic gel 0.25–0.5%, 1 drop daily
timolol 0.5% with dorzolamide 2%	Cosopt	Ophthalmic sol 1 drop bid
betaxolol	Betoptic-S	Ophthalmic susp 0.25%, 1 drop bid
carteolol	Ocupress	Ophthalmic sol 1%, 1 drop bid
levobunolol	Betagan	Ophthalmic sol 0.5%, 1 drop bid
Alpha Agonists		
brimonidine	Alphagan-P	Ophthalmic sol 0.1%, 0.15%, 0.2%; 1 drop tid (8 h apart)

(*Continued*)

Table 18-2 Antiglaucoma Agents (*Continued*)

Generic Name	Trade Name	Dosage
brimonidine 0.2% with timolol 0.5%	Combigan	Ophthalmic sol 1 drop q12h
Prostaglandin Analogs		
bimatoprost	Lumigan	Ophthalmic sol 0.01%, 0.03% 1 drop at qPM
latanoprost	Xalatan	Ophthalmic sol 0.005%, 1 drop at bedtime
travoprost	Travatan-Z	Ophthalmic sol 0.004%, 1 drop at bedtime
tafluprost	Zioptan	Ophthalmic sol 0.0015%, 1 drop at bedtime
latanoprostene	Vyzulta	Ophthalmic sol 0.024%, 1 drop at bedtime
Rho kinase inhibitors		
netarsudil	Rhopressa	Ophthalmic sol 0.2%, 1 drop in the evening

[a] This brand name is no longer marketed, but the name is still commonly used.

[b] Constrict the pupil.

[c] Wide variation in strengths available. Check carefully for correct percentage.

Note: Other antiglaucoma agents and combination drugs are available. This is a representative list.

Mydriatics

Mydriatics (e.g., atropine) are used topically to *dilate the pupil* for ophthalmic examinations. Atropine also acts as a **cycloplegic** (paralyzes the muscles of accommodation). It is the drug of choice in eye examinations for children. However, other mydriatics, for example, cyclopentolate, are more often used for adults because of faster action and faster recovery time.

Side effects of mydriatics, more likely in older adult patients, may include:

! Increased IOP
Local irritation, tearing, and burning sensation (transient)
! Blurred vision (common)
Flushing, dryness of skin, and fever
Decreased salivation and sweating
Confusion (caution in older adults)

Cautions or contraindications for mydriatics apply to:

Angle-closure glaucoma
Infants

Phenylephrine is an alpha-sympathomimetic that produces mydriasis without cycloplegia. Side effects and cautions or contraindications are similar to those of epinephrine.

Patient Education

Patients being treated with mydriatics should be instructed regarding:

- Administering by closing tear duct after instillation (refer to Figure 18-2)
- Using aseptic technique to prevent contamination of the medicine
- Expecting blurred vision and sensitivity to light (wear dark glasses or stay out of bright light)

Local Anesthetics

Local ophthalmic anesthetics, such as tetracaine (*TetraVisc*), are applied topically to the eye for minor surgical and diagnostic procedures, removal of foreign bodies, or painful injury.

Side effects of local anesthetics are rare, except with prolonged use, but may include *hypersensitivity* (transient stinging) reactions such as *anaphylaxis in those allergic to the "-caine" local anesthetics* (ester type).

Contraindicated for prolonged use because of the danger of corneal erosions, delayed wound healing, and keratitis.

Refer to Table 18-3 for a summary of the mydriatics and local anesthetics for the eye.

Table 18-3 Mydriatics and Local Anesthetics for the Eye

Generic Name	Trade Name	Dosage	Comments
Mydriatics[a]			
atropine	Isopto Atropine	Oint, sol 1%	Administered 60 min before exam
cyclopentolate	Cyclogyl	Ophthalmic sol, 0.5%, 1%, 2%[b]	Check carefully for percent
phenylephrine	Mydfrin	Ophthalmic sol, 2.5%, 10%	
Local Anesthetics			
tetracaine	TetraVisc	Sol, 0.5%	Apply eye patch
proparacaine	Alcaine	Sol, 0.5%	Apply eye patch; store product in refrigerator

[a] Dilate the pupil.

[b] Wide variations in strengths are available. Check carefully for correct percentage.

Patient Education

Patients given local ophthalmic anesthetics should be instructed regarding:

- Necessity of wearing an eye patch after the use of tetracaine because of the loss of the blink reflex
- Avoidance of touching or rubbing the eye until the anesthesia has worn off
- Making certain the correct medication and correct percent solution are used as prescribed; there is a potential for certain eye drops to be prescribed for use in the ears, but ear drops should never be used in the eyes
- Continuing glaucoma treatment for a lifetime and having regular eye exams to prevent future vision damage
- Proper aseptic technique and handwashing to prevent contamination of the other eye, the dropper, or the ointment tube
- Instillation of the *correct number of drops* or amount of ointment into the conjunctival sac in the proper order (refer to Figure 18-1); if the directions say to use 2 drops, wait for 5 min before putting another drop into the same eye
- Closing the eye gently so as not to squeeze the medication out; using a tissue to gently blot extra medication coming out of the eye
- Applying gentle pressure to inner canthus after instillation to minimize systemic effects (refer to Figure 18-2); do not rub the eyes
- Avoiding use of an eyecup as an aid to administration due to the risk of contamination
- Monitoring storage requirements such as refrigeration and expiration dates closely (depending on the health care setting, eye medications may be assigned a shorter expiration date)—do not use outdated medication
- Keeping eye preparations out of the reach of children; most of these products are not originally provided in child-resistant packaging

Otic (Ear) Medications

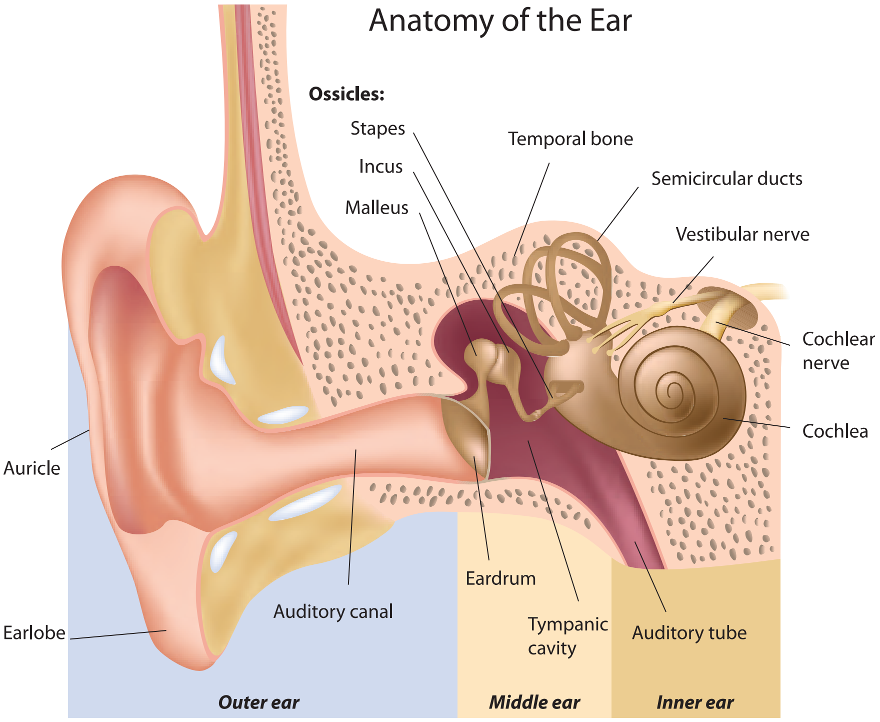
The ear is made up of three parts: the outer, middle, and inner ear (Figure 18-4). Together these parts serve two main purposes: hearing and balance. When either of these functions is disrupted, it is usually a sign that there is inflammation or blockage in one or more parts of the ear. There are two main categories of common ear conditions: (1) ear infections and (2) earwax build-up. These two types of conditions generally involve only the outer and middle ear and will be the focus of this section. Other, more serious, conditions of the ear involve the inner ear. They are more difficult to treat and often require the care of an ear, nose, and throat specialist.

Otitis Media

Otitis media (ear infection) occurs most commonly in children but can also occur in adults. It is most commonly caused by bacteria in the middle ear, which leads to inflammation (otitis media). In general, ear infections present with symptoms of pain (dull pulsing to sharp stabbing), tenderness, a feeling of “fullness” in the ear, fever, and difficulty hearing. It should be noted that infants and small children who cannot talk yet often become fussy and cry while reaching toward the affected ear. This is an indicator that they may have an ear infection. Treatment for ear infections can be broken down into topical and systemic medications. Treatment always involves an antibiotic that can sometimes be paired with a steroid (topical) or NSAID (systemic) for inflammation and pain.

Topical Preparations for Ear Infections

Cipro (ciprofloxacin), Floxin (ofloxacin), and Cortisporin (polymixin B, neomycin, and hydrocortisone) are the most commonly used topical antibiotics. Cipro is also available in two combination formulations (Ciprodex and Cipro HC), which contain a steroid. Topical otic antibiotics are best suited for outer ear infections (“swimmer’s ear”). In general, ear drops are well tolerated, but minor side effects



Alila Medical Media/Shutterstock.com.

Figure 18-4 The ear contains many small structures that contribute to hearing and balance. Notice how inflammation or blockage would disrupt these functions.

include irritation of the ear or burning and stinging when administering the drops. Treatment is usually prescribed for 7–14 days, and as always, the patient should be instructed to continue to use the drops for the entire time, even after symptoms have begun to improve or resolve.

There are also drops that are designed to treat only the pain and inflammation associated with an ear infection, and these are always paired with an antibiotic (otic or systemic). These medications are Vosol HC (acetic acid and hydrocortisone) and OTC homeopathic preparations. Vosol HC does contain an antibacterial (acetic acid), but it is not an antibiotic and should not be used to eradicate an established infection. Patients using OTC homeopathic ear drops should be instructed to use them only as temporary relief until they can be seen by a physician. It should be noted that the technique for proper administration of ear drops is different in children and adults.

Clinical Application

Eye Drops for Ear Drops

Oftentimes a patient will present to the pharmacy with a prescription for a topical **otic** (ear) antibiotic. Although it may seem incorrect, it is common practice to substitute an ophthalmic preparation (of the same active ingredient and concentration) if the pharmacy does not have the otic preparation in stock or it is not commercially available, if the otic preparation is not covered under the patient's insurance, or if the patient does not have insurance (ophthalmic preparations are generally less expensive). In these cases, the patient should be counseled that even though the bottle is labeled "ophthalmic," it is intended for "otic" use. Additionally, it should be noted that although you can use ophthalmic drops in the ears, you cannot use otic drops in the eyes. This is because while all ophthalmic drops must be formulated with a pH that is acceptable for use in the eyes (around 7.4), otic drops are not pH balanced or buffered. If an otic preparation were to be used in the eye, extreme burning and irritation would occur.

Systemic Preparations for Ear Infections

When the inner ear is involved, or when patients' compliance or proper drop technique is a concern (e.g., in older adults or young children), systemic antibiotics and NSAIDs are preferable over topical preparations. Amoxicillin and Augmentin are the most commonly used antibiotics for otitis media. They are both available in a liquid suspension and an oral tablet. Other antibiotics used are cephalosporin medications such as cephalexin and cefdinir. NSAIDs are usually paired with these systemic antibiotics to help alleviate pain and inflammation associated with the ear infection. They are also available as liquid suspensions or in oral tablet form.

Earwax Build-up and Blockage

When earwax accumulates in the ear canal, it can inhibit hearing and can cause pain. This type of condition is most commonly seen in older adults who may not be able to properly groom themselves or in patients who are prone to producing more earwax than normal. Earwax build-up can directly lead to a blockage, but it is more common that a blockage occurs as a result of the patient attempting to remove the earwax with a cotton swab or other object, which frequently results in the earwax being pushed deeper into the ear canal. Debrox (carbamide peroxide) is an OTC medication used to soften, loosen, and remove excessive earwax. If a patient is not successful after using this product, an ear, nose, and throat specialist must be consulted.

Refer to Table 18-4 for a list of medications used for ear infections and earwax build-up.

Table 18-4 Otic Preparations and Medications for Earwax Build-up

Generic Name	Trade Name	Dosage	Comments
Topical Antibiotics			
ciprofloxacin	Cipro	Otic sol, 0.2%, 3–4 drops bid for 7–14 days	Always use proper drop technique
ofloxacin	Floxin	Otic sol, 0.3%, 10 drops bid for 7–14 days	Often substituted with 0.3% ophthalmic drops
Combination Topical Antibiotics and Steroids			
ciprofloxacin and dexamethasone	Ciprodex	Otic sol, 0.3%/0.1%, 4 drops bid for 7 days	Always use proper drop technique
ciprofloxacin and hydrocortisone	Cipro HC	Otic sol, 0.2%/0.1%, 3 drops bid for 7 days	
polymixin B, neomycin, and hydrocortisone	Cortisporin	Otic sol, 4 drops q6–8h	
Topical Analgesics and Anti-inflammatory Agents			
acetic acid and hydrocortisone	Vosol HC	Otic sol, 1%/2%, 3–5 drops 4–6 times daily prn	Combination corticosteroid and antibacterial agent
Agents for Earwax Build-up			
carbamide peroxide	Debrox	Otic sol, 6.5% and 10%, 5–10 drops bid, max of 4 days (then consult ENT specialist)	Keep drops in ear for several minutes by tilting heading sideways and placing cotton in ear

Case Study A

Eye Medications

A patient who is aging has been experiencing a gradual loss of vision and they were recently diagnosed with chronic (open-angle) glaucoma.

1. The ophthalmologist explains to the patient that glaucoma is a condition that results from
   a. bleeding into the aqueous humor space
   b. obstruction of the outflow of the aqueous humor
   c. hyperpigmentation of the aqueous humor
   d. dehydration of the aqueous humor

2. The primary action of drugs for glaucoma is to
   a. increase intraocular pressure
   b. decrease intraocular pressure
   c. decrease external ocular pressure
   d. increase external ocular pressure

3. The physician explains that the treatment will
   a. be short term (1–3 months)
   b. be intermittent
   c. continue for 6–12 months
   d. continue for the patient's lifetime

4. The physician determines that the best medication to treat the patient is a carbonic anhydrase inhibitor, which acts by
   a. decreasing the formation of aqueous humor
   b. increasing blood flow to the aqueous humor space
   c. reducing aqueous humor inflammation
   d. decreasing blood flow to the aqueous humor space

5. The physician starts acetazolamide at a low dose but explains that the dose may need to be increased. If the dose is increased, the patient may experience which side effect?
   a. hyperactivity
   b. urinary tract infection.
   c. taste alteration
   d. urinary retention

Case Study B

Eye Medications

A person has been hit in the eye with a tennis ball and is experiencing severe pain.

1. Which medication would most likely be given to the patient to act as a local ophthalmic anesthetic?
   a. tetracaine
   b. atropine
   c. cyclopentolate
   d. phenylephrine

2. The physician applies a local ophthalmic anesthetic. What side effect may the patient experience?
   a. twitching of the eyelid
   b. anaphylaxis
   c. flushing of the eye's blood vessels
   d. profound itching

3. After being administered Alcaine, the nurse should instruct the patient to
   a. store the medication at room temperature
   b. remain upright for 2 h
   c. massage the eye every 4 h
   d. wear an eye patch

(*Continued*)

4. What will the nurse instruct the patient to do after self-administering eye drops?

a. blink rapidly

b. pull down her lower eye lid to let the excess medication drain out

c. apply pressure to her eyelid

d. close the eye gently so as not to squeeze the medication out

5. The patient is cautioned to follow up with their physician if the pain continues. This is because prolonged use of an ophthalmic anesthetic can cause which complication?

a. retinal detachment

b. cataract formation

c. corneal erosion

d. conjunctival bleeding

Chapter Review Quiz

Match the medication in the first column with the condition that it is used to treat in the second column. Conditions may be used more than once.

Medication

1. ______ Cosopt

2. ______ Acular

3. ______ tetracaine

4. ______ atropine

5. ______ prednisolone

6. ______ pilocarpine

7. ______ Timoptic

8. ______ Diamox Sequels

9. ______ Travatan Z

10. ______ phenylephrine

Condition

a. To dilate pupils

b. Glaucoma

c. Allergic reaction of eyes

d. Postoperative inflammation

e. Eye injury pain

Choose the correct answer.

11. The purpose of an ophthalmic decongestant medication is

a. to block histamine receptors

b. blood vessel vasoconstriction

c. to block the tear duct

d. blood vessel vasodilation

12. What is the best form of ophthalmic medication for adults?

a. gel

b. ointment

c. drops

d. medicated patch

13. When administering more than one ophthalmic medication at a time, the minimum amount of time desired between the medications is

a. 5 min

b. 15 min

c. 30 min

d. 1 h

14. Which category of drug may exacerbate glaucoma?

a. anticoagulant

b. anti-inflammatory

c. antihypertensive

d. anticholinergic

15. Which medication is used at the end of an eye exam to constrict the pupil?

a. timolol

b. atropine

c. pilocarpine

d. brimondidine

16. What should patients using OTC ear drops for pain relief be told?

a. Only use the drops for short-term relief until you can be seen by a physician.

b. Use the drops for as long as it takes to resolve the pain.

c. OTC otic drops can resolve a minor ear infection.

d. There is no specific patient counseling.

17. Patients who have earwax build-up should be instructed to

a. do nothing it will resolve on its own

b. attempt to remove it with a cotton swab

c. use an antibiotic drop from a past ear infection

d. use Debrox OTC

18. You can use otic drops in the eyes, but you cannot use ophthalmic drops in the ears.

a. True

b. False

Chapter 19

Central Nervous System Drugs: Analgesics, Sedatives, and Hypnotics

Key Terms and Concepts

Adjuvant analgesic
Analgesics
Antimigraine agents
Antipyretic
Coanalgesics
Dependence
Endorphins
Hypnotics
Medical marijuana
Opioid agonists
Opioid antagonist
Opioid-induced constipation (OIC)
Opioids
Orexin antagonists
Paradoxical
Placebo effect
Sedatives
Subjective
Tinnitus
Tolerance

Objectives

Upon completion of this chapter, the learner should be able to:

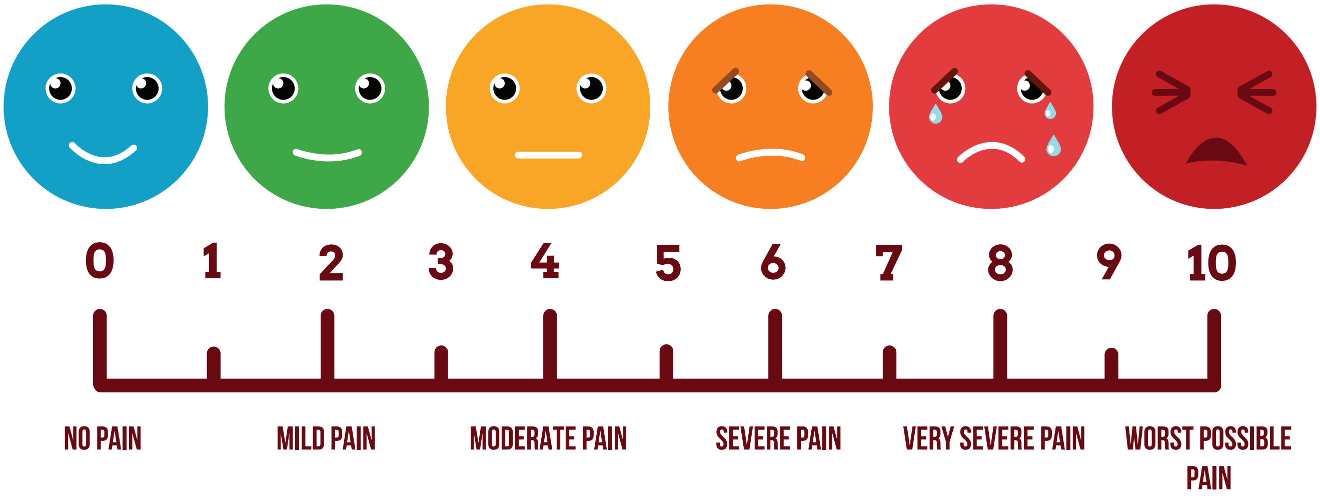
1. Explain the indications and actions of nonopioid, opioid, and adjuvant analgesics.
2. Analyze the role of sedatives and hypnotics in sleep.
3. List the side effects of the major analgesics, sedatives, and hypnotics.
4. Describe the information necessary for comprehensive patient education related to analgesics, sedatives, and hypnotics.
5. Explain the indications, side effects and contraindications of Antimigraine agents.

The central nervous system (CNS) has many functions. Analgesics, sedatives, and hypnotics depress central nervous system action to varying degrees. Some drugs can be classified into more than one category, depending on the dosage. This chapter will focus on the following categories of CNS medications:

- **Analgesics** given to relieve pain
- **Adjuvant analgesic** medications given to enhance the effects of analgesics
- **Antimigraine agents** given to prevent or relieve migraine headaches
- **Sedatives** given to calm, soothe or produce sedation
- **Hypnotics** given to produce sleep

Analgesics

The most common reason patients seek medical care is pain. The four most common types of pain reported by the National Center for Health Statistics are lower back, neck, migraine, and facial or jaw pain. Pain is **subjective** (i.e., it can be experienced or perceived only by the individual person). Health care professionals can assess a patient's pain by asking the patient to describe the pain and its location, and they assess the pain's severity by using validated pain assessment scales. These scales are often based on a range of 1–10, or use symbolic facial expressions to show level of pain (Figure 19-1).



MicroOne/Shutterstock.com.

Figure 19-1 Pain scales are used by health care professionals to assess pain at time of admission and to assess changes in pain levels.

Pain has both psychological and physiological components. Some people have a higher pain threshold than others because of conditioning, sensitivity, or physiological factors (e.g., endorphin release). **Endorphins** are analgesics produced within the body (endogenous) as a reaction to severe pain or intense exercise (e.g., "runner's high"). Endorphins block the transmission of pain. Endorphin release may be responsible for a **placebo effect**: relief from pain as the result of suggestion without the administration of an analgesic.

Opioid Analgesics

Opioids, also called **Opioid agonists** are classified as full (pure) agonists, partial agonists, or mixed agonist–antagonists depending on their activity at the receptor. Full agonists (e.g., morphine, hydromorphone, oxycodone, and fentanyl) are commonly used because their action is similar to that of opium in altering the perception of pain, and they do not have a ceiling to their analgesic effects. This means that there is no plateau to the amount of analgesic relief; the only limiting factor is side effects from higher doses. Because of their potential for abuse and psychological dependence, all **opioids** are classified as controlled substances by the FDA and their use should be limited when possible. When using opioids to treat pain, physicians generally attempt to do so with the lowest effective dose. They also add on adjuvant therapies to allow for lower opioid doses or use alternative therapy to avoid opioid use when possible.

When used chronically, opioids tend to cause **tolerance** (i.e., a larger dose of opioid is needed to achieve the same level of analgesia) and physiological **dependence** (i.e., physical adaptation of the body to the opioid and withdrawal symptoms after abrupt drug discontinuation). Addiction or psychological dependence is usually not a problem for patients who require opioids for short-term, acute pain management. Most people stop taking opioids when their pain resolves. Because of tolerance, the potential for developing dependence, and the potential for developing undesirable side effects, opioids are generally not used for extended periods, except to relieve chronic pain, for example, cancer pain, terminal illness, and nonmalignant pain in selected patients who do not benefit from other pain relief methods.

Adequate pain control is important for the terminally ill. Dependence is irrelevant for dying patients and should not be a consideration. More effective pain control can be achieved by combining opioids with nonopioid and adjuvant drugs. Analgesics should be given to terminally ill patients with constant *around-the-clock* pain, with additional "as-needed" doses for breakthrough pain. Dosages should be adjusted to achieve pain relief with an acceptable level of side effects. Around-the-clock dosing prevents pain from developing and is normally given in an extended-release (ER) formulation such as a patch or ER tablet or capsule. PRN, or as-needed, dosing is used for breakthrough pain only, and is available to patients as immediate-release (IR) formulations in the form of tablets, capsules, lozenges, or solutions.

Chronic pain therapy, for example, for back pain, sometimes includes the addition of a tricyclic antidepressant or anticonvulsant to the analgesic regimen. These drugs that enhance analgesic effects are called *adjuvant* analgesics and are explained later in this chapter. This addition can increase effectiveness of pain relief while also reducing the needed dosage of opioids.

Side effects of opioids can include:

- ❗ Sedation, confusion, and dizziness
- ❗ Hypotension and bradycardia
- ❗ Nausea and vomiting (usually resolves within a few days) and constipation (occurs in more than 50% of patients and frequently requires treatment)
- ❗ Respiratory depression (appropriate dose titration reduces risk)
- ❗ Physical and/or emotional dependence; tolerance

Cautions or contraindications with opioids apply to:

Head injury (i.e., conditions associated with increased intracranial pressure)
Cardiac disease (methadone has been associated with QT prolongation, which causes a cardiac arrhythmia that can be fatal in some patients) and hypotension
CNS depression
GI, hepatic, renal, and thyroid diseases
Chronic obstructive pulmonary disease (COPD) and asthma
Sleep apnea

Learning Hint

Think of chronic pain treatment in the same way as you feed yourself on a daily basis. In this case pain is equivalent to your hunger. Most people eat three large meals (breakfast, lunch, and dinner) spaced out evenly throughout the day. This is the same as the ER (extended-release) formulations of pain medication. In both cases their role is to control hunger or pain, respectively, throughout the day, but there will be times when a person has "breakthrough pain" or "breakthrough hunger." In these situations, the person can eat a snack or take a dose of IR (intermittent release) pain medication, respectively. So, the next time you wonder why a person on pain management needs both ER and IR formulations, just think of it in the same way as why you keep a candy bar or granola bar in your desk.

- Pregnancy and lactation
- Children
- Older adults and patients in a severely weakened state
- Driving or operating machinery (may impair mental or physical abilities)
- Individuals who may be prone to suicide ideation or substance abuse
- Opiate agonist hypersensitivity (can try an opioid from a different chemical class, with close monitoring)
- Abrupt drug discontinuation in patients taking opioids chronically

Interactions include potentiation of the effect of opioids with all CNS depressants, including:

- Psychotropics
- Alcohol
- Sedatives and hypnotics
- Muscle relaxants
- Antihistamines
- Antiemetics
- Antiarrhythmics or antihypertensives

Preoperatively, an opioid like fentanyl is usually administered parenterally before the start of anesthesia, according to the directions of the anesthesiologist. Meperidine is not recommended for routine use owing to a metabolite that may accumulate and cause seizures in patients with kidney disease, although it is useful for the treatment of postop shivering. Morphine and hydromorphone are commonly used to manage moderate to severe pain due to their longer duration of effect and potency. Hydromorphone is four to eight times more potent than morphine, so caution is necessary to avoid medication errors. Ketamine is used clinically to induce sedation and immobility in emergency or surgical scenarios, relieve pain, and cause amnesia (no memory of events while under the influence of the drug). More recently, it has been used in small doses to treat resistant depression.

Clinical Application

Opioid-Induced Constipation

Although opioids are very effective for providing pain relief, they also have various dose-related side effects that can make taking them challenging. Of the previously discussed side effects, only constipation is not self-limiting. This means that all other side effects will improve over time as a patient continues therapy, but **opioid-induced constipation (OIC)** does not. OIC occurs because the digestive tract contains similar receptors (mu-receptors) that are targeted in pain relief. When these receptors in the digestive tract are activated, transit time through the bowel is slowed and constipation occurs. Oftentimes an OTC stool softener or a stimulant laxative is sufficient, but in more severe cases prescription-strength medication is needed. Amitiza, Resistor, and Movantik are all medications used to treat severe OIC. Patients should also be instructed to stay hydrated and not remain stationary if possible. This is an important consideration for patients receiving opioid pain therapy, especially because it is often overlooked until OIC has already become an issue.

Note

The **opioid antagonist** (reversal agent) naloxone (also known as Narcan) is used in the treatment of opioid overdoses and in the operating room, delivery room, and newborn nursery for opiate-induced respiratory depression. Many states now have standing orders allowing pharmacists to dispense Narcan to any patient without a prescription from their doctor to combat the opioid crisis and overdoses. Naltrexone (ReVia), a pure opioid antagonist, and sublingual buprenorphine, a partial opioid antagonist, are used separately and together (Suboxone) in the treatment of opioid dependence.

Opioid agonists, more commonly known just as "opioids," are available in various strengths, as concentrated oral solutions and in combination products. Manufacturers are limited to using no more than 325 mg of acetaminophen (Tylenol) per dosage form to reduce the risk of severe liver injury associated with acetaminophen. Carefully note the product and strength to be administered. Opioids are also available in combination with NSAIDs (non-steroidal anti-inflammatory drugs) among others.

Hydrocodone-containing products are some of the most commonly prescribed pain medications in the United States. These products also consistently rank among the most abused drugs (along with oxycodone) in the United States each year according to the Drug Enforcement Agency (DEA) and are therefore classified as schedule II. Additionally, hydrocodone is now available in non-acetaminophen-containing formulations such as Zohydro ER and Hysinglia ER. Both abuse-deterrent formulations are indicated for around-the-clock maintenance pain relief.

Tramadol

Tramadol (Ultram) is a centrally acting synthetic analog of codeine with only partial action at the pain receptors. Since tramadol is only a partial opioid agonist, it provides less pain relief than other opioids, but also has less potential for abuse or respiratory depression (although both may occur) and is currently a Schedule III controlled substance. However, doses above the normal therapeutic range produce several negative side effects.

Tapentadol (Nucynta) was developed to take advantage of the positives associated with tramadol, with fewer of its negatives. Tapentadol's mechanism of action is considered to be a mixed opioid agonist, meaning it is an agonist at the pain receptors while also inhibiting the reuptake of norepinephrine. Tapentadol is classified as a Schedule II controlled substance and is used primarily for chronic pain.

Note

By inhibiting reuptake, the substance (such as serotonin) will be around longer and therefore have a greater effect.

Side effects and **Cautions** of tramadol and tapentadol are similar to the opioids listed previously. It should also be noted that tramadol can lower the seizure threshold, so it may not be a good option in patients who have experienced a head trauma from an accident.

Interactions of tramadol and tapentadol occur with:

Monoamine oxidase inhibitors (MAOIs) or neuroleptics (may increase seizure risk)

Carbamazepine (Tegretol) (antagonizes tramadol action)

Selective serotonin reuptake inhibitors (SSRIs) (especially Paxil, Zoloft), tricyclic antidepressants, and triptans (may cause serotonin syndrome and increase seizure risk)

Refer to Table 19-1 for a summary of the opioid analgesics.

Table 19-1 Opioid Analgesics[a]

Generic Name	Trade Name	Dosage	Uses/Comments
butorphanol	Stadol[b]	1–4 mg IM, or 0.5–2 mg IV, or 1 mg (one spray) nasal spray q3–4h PRN	Moderate to severe acute pain (e.g., migraine)
codeine		15–60 mg PO q4h PRN	Mild to moderate acute, chronic, and cancer pain
		PO 10–20 mg q4–6h PRN (max 120 mg per day)	Antitussive dose
with acetaminophen[c]	Tylenol with Codeine	15–60 mg codeine PO q4–6h PRN	Max 360 mg codeine and 4 g acetaminophen per day from all sources
fentanyl citrate	Actiq (loz) Fentora (buccal)	PO 200–400 mcg q4–6h PRN	Moderate to severe acute, chronic, or cancer pain
	Sublimaze[b]	25–100 mcg slow IV/IM	
fentanyl transdermal	Duragesic	Topical patch 12.5–100 mcg/h applied q2–3d	Duragesic patches should not be cut Patches should be disposed of safely since excess drug remains
hydrocodone with acetaminophen[d]	Lorcet Lortab Vicodin	PO 2.5–10 mg of hydrocodone (tab or liquid) q4–6h PRN	Moderate acute, chronic, or cancer pain, or antitussive; max 4 g acetaminophen per day
hydrocodone	Zohydro ER Hysinglia ER Vantrela ER	10–50 mg q12h 20–120 mg q24h	Abuse deterrent formulations Do not contain acetaminophen
hydromorphone	Dilaudid Exalgo	PO 2–4 mg q4–6h PRN IM, IV, SQ 0.2–1 mg q2–4h PRN R 3 mg q6–8h PRN	Moderate to severe acute, chronic, or cancer pain
meperidine	Demerol	50–150 mg PO/IM/IV/SQ, q3–4h PRN	Short-term for moderate to severe *acute* pain

(*Continued*)

Table 19-1 Opioid Analgesics (*Continued*)

Generic Name	Trade Name	Dosage	Uses/Comments
methadone	Dolophine Methadose	2.5–10 mg IM/IV/SQ/PO initially q8–12h PRN; maint. 5–20 mg PO q6–8h PRN	Severe chronic and cancer pain; also for narcotic withdrawal
Morphine Sulfate			
immediate release	morphine	PO 10–30 mg or PR 10–20 mg q3–4h PRN; IV (over 4–5 min); IM/SQ 2.5–15 mg q2–6h PRN	Moderate to severe acute, chronic, or cancer pain
extended release	MS Contin (tab) Avinza (cap) Kadian (cap) Morphabond (tab)	PO, R 15–100 mg q8–12h PO 30 mg q24h (initially, titrate to response) PO 10 mg bid or 20 mg QD (initially, titrate to response) PO 15–100 mg bid	Do not crush! OD can be fatal May open caps and sprinkle contents on applesauce; can give Kadian contents via a gastrostomy tube Morphabond is an abuse deterrent tablet; it cannot be crushed or broken
Oxycodone			
controlled release	Oxycontin oxycodone ER tablets (generic)	PO 10–80 mg SR q8–12h	Serious abuse potential, overdose can be fatal; do not crush
immediate release	Roxicodone oxycodone IR	PO 5–10 mg q6h PRN	Moderate to severe acute, chronic, or cancer pain
with aspirin[e]	Percodan	PO 1–2 tabs q4–6h PRN	Max 12 tabs per 24 h
with acetaminophen	Percocet Roxicet	PO 1–2 tabs q4–6h PRN	Max 4 g acetaminophen per day
tramadol	Ultram	PO 50–100 mg q4–6h PRN, max 400 mg daily	Weak opioid analgesic for acute pain; not controlled federally
	Ultram ER	PO 100–300 mg daily	Do not crush; for chronic pain
with acetaminophen	Ultracet	PO 2 tabs q4–6h PRN	Max 8 tabs per day; for acute pain
tapentadol	Nucynta	PO 50–100 mg q4–6h PRN	For moderate to severe acute pain
	Nucynta ER	PO 50–250 mg SR q12h	For moderate to severe chronic pain; do not crush

[a] Combination opioid products (check for allergies, especially aspirin combinations).

[b] This brand name is no longer marketed, but the name may still be used.

[c] Tylenol with codeine tabs contain 300 mg acetaminophen plus codeine;

#2 tab: 15 mg codeine, #3 tab: 30 mg, #4 tab: 60 mg (max acetaminophen dose 4 g/day).

acetaminophen with codeine elixir: 120 mg acetaminophen and 12 mg codeine per 5 mL.

[d] Norco, Vicodin, Lortab: 325 mg acetaminophen and 5 mg, 7.5 mg, and 10 mg hydrocodone, respectively.

Vicodin tabs: 300 mg acetaminophen and 5 mg hydrocodone.

Vicodin ES tabs: 300 mg acetaminophen and 7.5 mg hydrocodone.

Vicodin HP tabs: 300 mg acetaminophen and 10 mg hydrocodone.

Lortab elixir: acetaminophen and hydrocodone concentrations vary depending on the manufacturer.

[e] Percodan or Endodan tabs: 325 mg aspirin and 5 mg oxycodone.

Percocet, Roxicet, or Endocet: 325 mg acetaminophen and 5 mg oxycodone. (Other strengths are available.)

Nonopioid Analgesics

Nonopioid analgesics, many of which are available without a prescription as over-the-counter (OTC) medications, are very popular. Therefore, it is extremely important that the health care professional be informed and responsible for patient education in this very important area of public health. The public needs to become aware of the dangers of self-medication, overdosage, side effects, and interactions, as well as the danger of poisoning to children and older adults by inappropriate use of these readily available drugs.

Nonopioids are given for the purposes of relieving mild to moderate pain, fever, and inflammatory conditions, for example, arthritis. They are also used to help treat more severe pain to allow for lower doses of opioids to be used. When used in this context, they are termed **coanalgesics**. The salicylates (aspirin) are most commonly used for their *analgesic* and **antipyretic** (fever-reducing) properties, as well as for their anti-inflammatory action. Other anti-inflammatory drugs, for example, ibuprofen, are also used for their analgesic properties.

Acetaminophen has analgesic and antipyretic properties but very little effect on inflammation. Aspirin and acetaminophen are frequently combined with opioids (refer to Table 19-1) or with other drugs for more effective analgesic action. There are many other combination analgesic products available OTC. Patients should be instructed to check all ingredients in these combination products because of potentially serious adverse side effects, for example, aspirin allergy or acetaminophen contraindications. When patients are taking acetaminophen, it is important to instruct them that other products (including OTC medications) containing acetaminophen should not be used without the knowledge and approval of their physician or pharmacist.

Salicylates and Other NSAIDs

Salicylate analgesic and anti-inflammatory actions are associated primarily with preventing the formation of prostaglandins and the subsequent inflammatory response prostaglandins help to induce.

Side effects of salicylates and other NSAIDs, especially with prolonged use and/or high dosages, can include:

- ❗ Prolonged bleeding time and bruising
- ❗ Gastric distress, ulceration, and bleeding (which may be silent)
- ❗ **Tinnitus** (ringing or roaring in the ears) and hearing loss with overdose
- Renal insufficiency
- ❗ Gastrointestinal (GI) symptoms, which can be minimized by administration with food or milk or by using an aspirin buffered with antacids or in enteric-coated form

Cautions or contraindications for salicylates and other NSAIDs apply to:

- GI ulcer, bleeding, and bleeding disorders
- Asthma
- Children younger than 15 years with influenza-like illness (because of the danger of Reye's syndrome)

Treatment of pain with NSAIDs after heart surgery

Pregnancy and lactation

Pre- or postoperative conditions (discontinue 5 to 7 days before elective surgery)

Interactions of salicylates may also occur with NSAIDs and:

Alcohol (may increase potential for ulceration and bleeding)

Anticoagulants (potentiation)

Corticosteroids (gastric ulcer)

Antacids in high doses (decreased effects)

NSAIDs (decreased effects, increased GI side effects)

Do not give salicylates and NSAIDs together (unless approved by a physician)

Insulin or oral antidiabetic agents (increased effects; may interfere with certain urinary glucose tests)

Methotrexate (increased effects)

Probenecid (decreased effects)

Antihypertensives: angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and diuretics (decreased effects)

Carbonic anhydrase inhibitors (toxic effects, e.g., Diamox)

Note

Acetaminophen (Tylenol) is frequently combined with opioid analgesics when stronger pain relief is required. Some examples of such combinations include Tylenol #3, Lorcet, Lortab, Vicodin, Percocet, and Roxicet. For examples of other opioid combinations and for information regarding the proportion of the ingredients in each product, refer to Table 19-1 and the combination opioid products footnote below the table. Remember, all opioids are federally controlled substances.

Acetaminophen

Acetaminophen (Tylenol) is used extensively in the treatment of mild to moderate pain and fever. It has very little effect on inflammation. However, acetaminophen has fewer adverse side effects than the salicylates (e.g., does not cause gastric irritation or precipitate bleeding). Therefore, it is sometimes used only for its analgesic properties in treating the chronic pain of arthritis so that the salicylate dosage may be reduced to safer levels with fewer side effects in these patients.

Side effects of acetaminophen are rare, but large doses can cause:

❗ Severe liver toxicity—higher risk at higher doses or in patients with previous hepatic impairment

Caution must be used with frequent acetaminophen use and alcohol ingestion because of potential liver damage.

Contraindicated with hypersensitivity to acetaminophen or any component of the combination product.

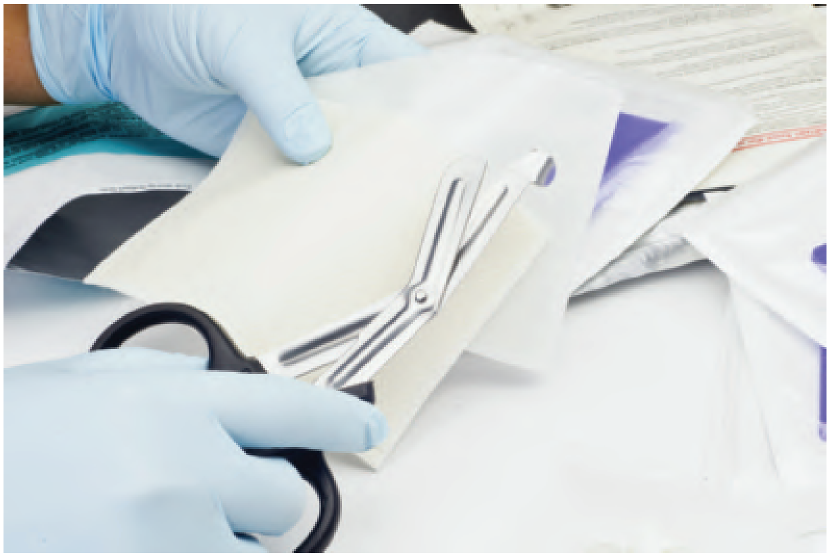
Local Anesthetics

The lidocaine patch (Lidoderm) is approved for the management of postherpetic neuralgia, although it can provide significant analgesia in other forms of neuropathic pain, including diabetic neuropathy and musculoskeletal pain such as osteoarthritis and lower back pain. Topical lidocaine provides pain relief through a peripheral effect and generally has little if any central action. Local creams, jellies, gels, and ointments are used to temporarily treat pain (like a cold sore or sore in the mouth) as a numbing agent. They can also be used as a numbing agent for minor procedures like the removal of skin tags or moles.

The lidocaine patch must be applied to intact skin. To reduce the potential for serious adverse effects and the development of tolerance, patches are worn only once for up to 12-h within a 24-h period and then removed. If these patches are not removed for a 12-h period, tolerance may develop, and the patch will be rendered ineffective. It may take up to 2 weeks to achieve the desired outcomes. It should be noted that although many patches cannot be cut, lidocaine patches are able to be cut into smaller custom-sized pieces (Figure 19-2).

Note

Sometimes a local vasoconstricting agent such as epinephrine is given in conjunction with a local anesthetic injection such as lidocaine to further help localize the effect and thereby prolong the duration of the effect.



Sherry Yates Young/Shutterstock.com.

Figure 19-2 Lidocaine patches provide local pain relief, so it is convenient for patients to be able to cut them to cover exactly the area that they need treated.

Side effects of the lidocaine patch, local in nature, are generally mild and transient and include:

- ! Erythema, edema, and hives
- ! Allergic reactions

Cautions or contraindications for the lidocaine patch apply to:

Sensitivity to local anesthetics
Nonintact skin
Pregnancy, breastfeeding, and pediatric use
Handling and disposal to prevent access by children or pets

Drug interactions of the lidocaine patch occur with:

Antiarrhythmic drugs such as mexiletene
Local anesthetics

Medical Marijuana

Medical marijuana refers to the use of legally prescribed cannabis or its synthetic derivatives (cannabinoids) to treat a disease with symptoms of chronic pain, nausea, and severe decreased appetite. It can also refer to traditional marijuana use that is prescribed by a doctor. This type of treatment is subject to the laws and regulations of each state, where there is much variation. At one time, medical marijuana and cannabinoid treatments were considered as a treatment option only in end-of-life situations where palliative care is a priority, but it has become more common for physicians to prescribe medical marijuana for mental health conditions such as anxiety, posttraumatic stress disorder (PTSD), and depression. In these cases, dispensaries are available (in states that allow them) with licensed pharmacists specifically trained to counsel patients on medical marijuana use. Medical marijuana is administered in various methods, such as liquid tinctures, various forms of inhalation, and capsules by mouth (dronabinol) among others. In general, the cannabinoids are used for pain associated with cancer and other severe disease states, while the medical marijuana available at dispensaries is more common for mental health conditions and pain not associated with the end of life. Side effects include dizziness, feeling tired, increased appetite, and hallucinations.

Refer to Table 19-2 for representative examples of nonopioid analgesics and antipyretics, Local Anesthetics, Medical Marijuana and cannabinoids.

Table 19-2 Nonopioid Analgesics and Antipyretics, Local Anesthetics, Medical Marijuana and cannabinoids

Generic Name	Trade Name	Dosage	Uses/Comments
Nonopioid Analgesics and Antipyretics			
acetylsalicylic acid[a] (ASA, aspirin)	Ecotrin, Ascriptin, Bufferin	325–650 mg PO or rectal supp q4h PRN; larger doses for arthritis	Administer with milk or food; may cause Reye's syndrome in children and teenagers
acetaminophen	Tylenol (OTC)	325–650 mg PO or rectal supp q4h PRN (max 4 g/day) 160 mg/5mL PO liquid	No anti-inflammatory action; less effective than ASA for soft tissue pain New standard OTC liquid dose for children
	Ofirmev (Rx)	1 g IV q6h PRN or 650 mg q4h PRN (>50 kg) weight based for less than 50 kg	For mild to moderate pain, fever; for moderate to severe pain with adjunctive opioid analgesics
Combinations[b]			
ASA and caffeine	Anacin	2 tabs PO q6h PRN, max 8 per day	
ASA, acetaminophen, and caffeine	Excedrin	2 tabs/caps PO q6h PRN, max 8 per day	Also for the pain of migraine headaches
butalbital, caffeine, *with acetaminophen*	Esgic, Fioricet (Rx)	1–2 tabs/caps PO q4h PRN, max 6 per day	For tension headache or migraine
with aspirin	Fiorinal (C-III)		
Local Anesthetics			
lidocaine	Lidoderm Xylocaine AneCream Xolido	1–3 patches 5% daily (may be cut into smaller sizes) Topical jelly/cream 2% to 5%	For postherpetic neuralgia (on 12 h/off 12 h) Use for temporary relief of pain or as a numbing agent prior to minor procedures

Generic Name	Trade Name	Dosage	Uses/Comments
Medical Marijuana and Cannabinoids[c]			
nabilone	Cesamet	1 mg capsules bid	Also used for chemotherapy-induced nausea and vomiting
dronabinol	Marinol	PO 2.5, 5, 10 mg capsules bid	Also used for chemotherapy-induced nausea and vomiting

[a] Other nonsteroidal anti-inflammatory drugs with analgesic action are listed in Table 21-2.

[b] Representative sample.

[c] Medical marijuana products available at dispensaries are not listed due to variability in dosage and product availability.

Adjuvant Analgesics

Many drugs that are considered adjuvant analgesics were originally intended for the treatment of conditions other than pain but have shown effectiveness in reducing certain kinds of pain. *Adjuvant* analgesics may enhance the analgesic effect of opioids and nonopioids, produce analgesia alone, or reduce the side effects of analgesics. Nerve pain (neuropathic pain) can be caused by certain disease states (such as diabetic neuropathy), infections (such as postherpetic neuralgia), and medications (certain chemotherapeutic agents and antiretrovirals). Fibromyalgia is a condition characterized by chronic, widespread musculoskeletal pain; muscle tenderness; sleep disturbances; and profound fatigue.

Both neuropathic pain and fibromyalgia may not be adequately relieved by the pain medications discussed earlier. Two classes commonly used for analgesia in these conditions are anticonvulsants and specific classes of antidepressants. Another agent, lidocaine, has been discussed previously in this chapter, and may be especially effective in treating nerve pain.

Tricyclic Antidepressants

Tricyclic antidepressants are used in the treatment of fibromyalgia and nerve pain associated with herpes, arthritis, diabetes, and cancer; migraine or tension headaches; insomnia; and depression. Often, the patient will describe the pain as “burning.” Tricyclic antidepressant actions are associated with increasing available norepinephrine and serotonin, which blocks pain transmission. Drugs in this class commonly used for pain include amitriptyline, desipramine, and nortriptyline. Allow 2 to 3 weeks for therapeutic effects.

Side effects of tricyclic antidepressants (more so with amitriptyline) can include:

- ❗ Dry mouth, urinary retention, delirium, and constipation
- ❗ Sedation (take at bedtime)
- ❗ Orthostatic hypotension

The degree of side effects varies with each antidepressant. Side effects may be additive with opioids (e.g., increased constipation, hypotension, and sedation).

Cautions or contraindications for tricyclics apply to hypersensitivity and the recovery phase of myocardial infarction as well as other cardiac conditions.

Serotonin Norepinephrine Reuptake Inhibitors

Duloxetine (Cymbalta) and venlafaxine (Effexor XR) are antidepressants that inhibit the reuptake of both serotonin and norepinephrine. They do not affect histamine or muscarinic receptors like the tricyclics do; therefore, anticholinergic side effects are not present. The serotonin norepinephrine reuptake inhibitor (SNRI) antidepressants are used to treat diabetic neuropathy and fibromyalgia. Milnacipran (Savella), an SNRI with antidepressant activity, is indicated only for fibromyalgia.

Side effects of SNRIs include sleep disturbance, headache, nausea, stomach pain, diarrhea, constipation, dizziness, and sweating. Venlafaxine has the potential to increase blood pressure and heart rate.

Cautions or contraindications apply to narrow-angle glaucoma, hepatic (duloxetine, venlafaxine) and renal (milnacipran) impairment, abrupt discontinuation, patients with a history of suicidal ideation or behaviors, and substantial alcohol use.

Interactions with all SNRIs and serotonergics (such as MAOIs and SSRIs) may result in serotonin syndrome. Milnacipran has fewer interactions than the other SNRIs.

Anticonvulsants

Anticonvulsants (e.g., Neurontin and Tegretol), like tricyclic antidepressants, are commonly used for the management of nerve pain associated with neuralgia, herpes zoster (shingles), and cancer. Anticonvulsant therapy is implemented when the patient describes the pain as “sharp,” “shooting,” “shock-like,” or “lightning-like.”

Gabapentin (Neurontin) is generally considered a first-line *anticonvulsant* for neuropathic pain therapy, followed by carbamazepine (Tegretol) and lamotrigine (Lamictal). Carbamazepine is also indicated for trigeminal neuralgia (also known as tic douloureux), with symptoms that include episodes of facial pain, often accompanied by painful spasms of facial muscles.

Pregabalin (Lyrica), a compound that is chemically and structurally similar to gabapentin, is a second-generation anticonvulsant approved by the FDA for use in fibromyalgia, diabetic neuropathy, and postherpetic neuralgia. Pregabalin has been designated as a Schedule V controlled substance because of its potential for abuse and dependence. It is often used as a replacement for gabapentin if the patient has experienced adequate pain relief with gabapentin, but intolerable side effects.

Side effects of anticonvulsants can include:

- Sedation, dizziness, and confusion
- Hepatitis (not Lyrica)
- Rash, Stevens–Johnson syndrome (Lamictal—start low, with slow titration upward)
- Nystagmus, diplopia (double vision), and blurred vision
- Weight gain and peripheral edema (pregabalin)

Caution must be used with anticonvulsants if used with allergies, hepatitis, cardiac disease, or renal disease.

Caution

Do not confuse *Lamictal* (anticonvulsant) with *Lamisil* (antifungal).

Cautions or contraindications with anticonvulsants include:

Hypersensitivity
Psychiatric conditions (increased risk of suicidal ideation and behavior)
Pregnancy
❗ Abrupt discontinuation

Interactions of anticonvulsants occur with:

Alcohol (decreased effects)
Antacids (decreased effects) (Neurontin)
Antineoplastics (decreased effects) (Tegretol)
CNS depressants (decreased effects) (Tegretol)
Folic acid (decreased effects) (Lamictal)

Refer to Table 19-3 for a summary of adjuvant analgesics.

Table 19-3 Adjuvant Analgesics

Generic Name	Trade Name	Dosage[a]	Comments
Antidepressants			
Tricyclics			
amitriptyline	Elavil[b]	PO 10–150 mg at bedtime	Use with caution in older adults
nortriptyline	Pamelor	PO 10–150 mg at bedtime	Both of these are less likely to cause certain side effects vs. amitriptyline
desipramine	Norpramin	PO 10–150 mg at bedtime	
SNRIs[c]			
duloxetine	Cymbalta	PO 60–120 mg daily	
milnacipran	Savella	Titrate PO to 50–100 mg bid	For fibromyalgia only
venlafaxine	Effexor XR	PO 75–225 mg daily	
Anticonvulsants			
carbamazepine	Tegretol	PO 200–600 mg bid	Especially for trigeminal neuralgia; monitor serum levels periodically

(*Continued*)

Table 19-3 Adjuvant Analgesics (*Continued*)

Generic Name	Trade Name	Dosage[a]	Comments
gabapentin	Neurontin	PO 600–3,600 mg per day divided doses three to four times per day	For nerve pain, especially postherpetic neuralgia DEA considering adding schedule to gabapentin
lamotrigine	Lamictal	PO 25–200 mg bid	Slow titration to avoid rash
pregabalin	Lyrica	PO 150–600 mg per day in two to three divided doses	Slow titration to avoid rash (Stevens–Johnson syndrome); for fibromyalgia, diabetic neuropathy, and postherpetic neuralgia

[a] All adjuvants should be started at the lower end of the dosage range and titrated upward in small increments weekly according to the clinical response.

[b] This brand name is no longer marketed, but the name is still commonly used.

[c] Serotonin norepinephrine reuptake inhibitors.

Note: Please note this is a representative list of the more common adjuvant analgesics.

Antimigraine Agents

Migraine is the most common neurovascular headache and may include nausea, vomiting, and sensitivity to light or noise. Migraines (and most other forms of headache) respond best when treated early. Typically, patients who experience chronic migraines will have an aura before the migraine occurs that can help warn them a migraine is about to occur. Think of the aura like a warning siren used before a tornado to alert nearby residents a tornado may occur. Simple analgesics (refer to Table 19-2), NSAIDs, and opioid analgesics can be effective, especially if they are taken at the initial sign of migraine. Generally, opioids are reserved for refractory migraines that do not respond to other therapy options and are never considered first-line therapy.

Serotonin Receptor Agonists (SRAs)

For those patients unresponsive to the simple analgesics or NSAIDs, serotonin agonists were developed based on the observation that, as migraine symptoms worsen during an attack, serotonin levels decrease while vasodilation and inflammation of blood vessels in the brain increase. SRAs are also effective in treating the nausea and vomiting associated with migraines because serotonin receptors are also found in the gastrointestinal (GI) tract.

SRAs are indicated for the acute treatment of migraines in adults and are not FDA approved for the prophylactic management of migraine headaches. Nasal spray formulations may be useful if the patient has nausea and vomiting or cannot swallow tablets. Additionally, nasal spray formulations are absorbed more quickly by the body and therefore have a quicker onset. Individual responses to triptans vary; patients who do not respond to one triptan may respond to another. In general, these medications are taken at the onset of a headache (or first warning sign), and then repeated if needed in 2 h. Some triptans have alternative second dose schedules and some are not indicated for a second dose. Patients should be warned to not take more than recommended or prescribed in a 24-h period unless directed to do so by their physician.

iStock.com/fizkes.

Side effects of SRAs include:

- ❗ Malaise, fatigue, dizziness, and drowsiness
- Asthenia, tingling, paresthesias, and flushing
- ❗ Various cardiac complications

Cautions or contraindications with SRAs apply to:

- Patients with cerebrovascular or cardiovascular disease
- Uncontrolled hypertension
- Peripheral vascular disease
- Hepatic or renal disease (dose adjustments may be needed)
- Older adults (who are more likely to have decreased hepatic function and more pronounced blood pressure increases and are at risk for coronary artery disease)
- Pregnancy and lactation
- Children

Drug interactions of SRAs occur with:

- Ergot alkaloids (i.e., methylergonovine; additive vasospastic effects)
- MAOIs elevate the plasma levels of *most* triptans (do not use within 2 weeks of discontinuing the use of the MAOI)
- Most antidepressants potentiate the effects of serotonin (including SSRIs and tricyclics) and may result in serotonin syndrome (mental status changes, diaphoresis, tremor, hyperreflexia, and fever) when used in combination
- Macrolide antibiotics, antiretroviral protease inhibitors, and "azole" antifungals with eletriptan (increased plasma levels) (do not use within at least 72 h of each other)

Non-Triptan Agents for Migraine

Although triptans are the mainstay for acute migraine therapy, there are other medications used to treat and prevent migraines. These medications may belong to other classes and may be used off-label. For example, the beta-blocker propranolol, commonly used for heart conditions, is often used to help prevent migraines.

A new class of migraine-prevention therapies target the calcitonin gene-related peptide (CGRP) pathway, a protein linked to migraine symptoms. These monoclonal antibodies include erenumab (Aimovig), which works by blocking the CGRP receptor, while the other drugs in this class inhibit CGRP itself. These drugs are administered via injection or infusion. Other drugs in this class include galcanezumab (Emgality), fremanezumab (Ajovy) and eptinezumab (Vyepti). Side effects include injection site reactions, headache, and fatigue. As with most monoclonal antibodies, patients should be cautioned that their immune system may be weakened by these drugs and therapy may be contraindicated in those with certain chronic infections like HIV and hepatitis or those who are pregnant.

Gepants, an additional newer class of drugs, target CGRP as well but are provided orally. These medications include ubrogepant (Ubrelvy), rimegepant (Nurtec) and atogepant (Qulipta). Ubrelvy is used to help treat acute migraines, while Qulipta is used for migraine prevention, and Nurtec can be used for both. The most common side effects of gepants are nausea, sleepiness, and dry mouth. Patients should be cautioned in taking these drugs if they are also taking a CYP3A4 inhibitor drug like clarithromycin, erythromycin, diltiazem, itraconazole, ketoconazole, ritonavir, and verapamil. Grapefruit juice should not be consumed while taking gepants.

Lasmiditan (Reyvow) is a separate type of treatment that targets the serotonin receptors on brain nerve endings to halt migraine attacks as they occur. This drug class may be referred to as "diptans." Patients taking lasmiditan should be aware that dizziness, sedation, fatigue, and nausea are common side effects. Cautions include driving while on this medication or for up to 8h after taking a dose as significant motor and cognitive impairment can occur.

Refer to Table 19-4 for information on antimigraine agents.

Table 19-4 Antimigraine Agents

Generic Name	Trade Name	Dosage Forms	Initial Dose Adult	Repeat Time (Hours)	Daily Maximum Dose (mg)
Triptans					
almotriptan	Axert	Tablet	6.25–12.5 mg	2	25
eletriptan	Relpax	Tablet	20–40 mg	2	40
frovatriptan	Frova	Tablet	2.5 mg	2	7.5
naratriptan	Amerge	Tablet	1–2.5 mg	4	5
rizatriptan	Maxalt	Tablet	5–10 mg	2	30
	Maxalt-MLT	OD tablet	5–10 mg	2	30

Generic Name	Trade Name	Dosage Forms	Initial Dose Adult	Repeat Time (Hours)	Daily Maximum Dose (mg)
sumatriptan	Imitrex	SQ	4 mg, 6 mg	1	12
		Nasal	5–20 mg	2	40
		Tablet	25–100 mg	2	200
zolmitriptan	Zomig	Tablet	2.5–5 mg	2	10
	Zomig-ZMT	OD tablet	2.5–5 mg	2	10
	Zomig	Nasal	5 mg	2	10
Ditans					
lasmiditan	Reyvow	Tablet (Schedule V)	50–200 mg	n/a Do not repeat if ineffective Max 1 dose per 24 h	200

CGRP Blockers and Gepants

Generic Name	Trade Name	Dosing
erenumab	Aimovig	70 mg SQ monthly
galcanezumab	Emgality	120 mg SQ monthly
fremanezumab	Ajovy	225 mg SQ monthly 675 mg every 3 months
eptinezumab	Vyepti	100 mg IV every 3 months
ubrogepant	Ubrelvy	50–100 mg PO daily
rimegepant	Nurtec	75 mg PO daily
atogepant	Qulipta	10–60 mg PO daily

OD = orally disintegrating tablet.

Note: Representative sample; other products are available.

Sedatives and Hypnotics

Sedatives and hypnotics are medications used to promote sedation in smaller doses and promote sleep in larger doses. Insomnia is one of the most prevalent sleep disorders, with symptoms occurring in over 70 million U.S. adults, about 30% of the population. The prevalence of chronic insomnia is higher in females and older people. The sedative-hypnotics discussed in this section are classified as benzodiazepines (BZDs) and nonbenzodiazepines (non-BZDs). Some psychotropic drugs like trazodone and mirtazapine are also used as sedative-hypnotics.

Antihistamines—for example, diphenhydramine (Benadryl, Nytol, Sominex) and doxylamine (Unisom)—have an extended half-life, remaining in the system longer than other similar medications. Because of slower metabolism and impaired circulation, the older patient or patients in a severely weakened state are particularly susceptible to side effects, such as blurred vision, dizziness, hypotension, confusion, and decreased coordination. These effects can continue for a longer time, resulting in "morning-after" problems. Tolerance can develop to the sleep-inducing effect, but not to the side effects. Therefore, antihistamines are not as effective as other available sedative-hypnotics.

None of these medications should be used for extended periods of time (>10 days) except under close medical supervision because of the potential for psychological and physical dependence. In addition, these medications depress the REM (rapid eye movement, or dream) phase of sleep, and withdrawal after prolonged use can result in a severe rebound effect with nightmares and hallucinations. Abrupt withdrawal of hypnotics, even after short-term therapy (for example, one week) may result in rebound insomnia. Therefore, gradual reduction of dosage is indicated.

iStock.com/PeopleImages.

Before starting pharmacological treatment, patients should be encouraged to use nondrug interventions to combat insomnia. These include exercising during the day; avoiding daytime naps; avoiding heavy meals and activating medications near bedtime; and taking advantage of warm milk, back rubs, soft music, relaxation techniques, and other calming influences. In addition, avoiding caffeine and alcohol should be stressed. Alcohol may help to initiate sleep, but it results in early awakening.

Barbiturates are rarely used now as sedative-hypnotics because of the many serious, potentially dangerous side effects, especially CNS depression. Phenobarbital is still used in the treatment of seizure disorders. However, there are many other safer and more effective hypnotics available. Therefore, the use of barbiturates for sedation is restricted to specific limited circumstances in which the patient can be closely monitored (i.e., Brevital for general anesthesia induction and maintenance).

Benzodiazepines (BZDs) like temazepam (Restoril) and nonbenzodiazepines (non-BZDs) like zolpidem (Ambien) have supplanted barbiturates as sedative-hypnotics and have less potential for abuse. However, withdrawal effects are observed after long-term use, and respiratory depression (when taken with alcohol) can be potentially fatal. As mentioned earlier, the cause of insomnia should be established and underlying factors should be treated before a hypnotic is prescribed. Only short-term use (7–10 days) is recommended for most agents. Like BZDs, non-BZDs are classified as controlled substances because of the possibility of physical and psychological dependence.

Side effects of all the sedative-hypnotics can include:

- ❗ Daytime sedation, confusion, and headache—hangover
- ❗ Increased risk of falls (especially in older adults or with long-acting hypnotics)
- ❗ Dependence or withdrawal symptoms
- ❗ Sleepwalking and engaging in complex tasks (i.e., “sleep eating,” “sleep driving,” and “sleep sex”)

Cautions or contraindications for all the sedative-hypnotics apply to:

Severe renal impairment
Abrupt discontinuation
Older adults
Patients in a severely weakened state
Patients prone to addiction
Patients who are depressed and those with uncontrolled or untreated mental health disorders
Individuals who have suicidal ideation or behavior
Pregnancy and lactation
Children
COPD and sleep apnea

Interactions of all the sedative-hypnotics with the following drugs can be dangerous and potentially fatal:

Psychotropic drugs
Alcohol
Muscle relaxants
Antiemetics
Antihistamines
Analgesics

Melatonin Receptor Agonists

Ramelteon (Rozerem) was the first FDA-approved prescription medication that acts on melatonin receptors, mimicking the actions of melatonin to trigger sleep onset. As a result of this mechanism of action, dependence and abuse potential are eliminated, and ramelteon is not classified as a controlled substance.

Ramelteon and other melatonin receptor agonists (MRAs) (like Hetlioz) work quickly, generally inducing sleep in less than 1 h (give within 30 min of going to bed with a high-fat meal or snack). There have been no studies comparing the effectiveness of MRAs against other hypnotics or even against melatonin supplements. Dose reductions are not required in older adults; however, MRAs should be used with caution in patients with hepatic impairment.

The use of ramelteon is contraindicated with fluvoxamine (Luvox), which inhibits the metabolism of ramelteon. Do not use MRAs with melatonin because of the potential for additive sedative effects.

Orexin Antagonists

The FDA approved suvorexant (Belsomra) in 2014. Belsomra is part of a relatively new class of hypnotic drugs called **orexin antagonists**. These drugs function by blocking orexin A and B from binding to orexin receptors in the brain. Orexin A and B are chemicals that cause people to stay awake. Blocking these receptors allows for reduced wakefulness, increased duration of sleep, or increased ability to fall asleep. Other drugs called lemborexant (Dayvigo) and daridorexant (Quviviq) have been recently added to the orexin antagonist class.

Learning Hint

Think of orexin receptors (and all receptors) like parking spots in a parking lot. When you introduce a drug that binds to an orexin receptor and blocks it, the naturally occurring orexin in your body cannot bind to it. Just how if you were in a parking lot and all the spots were full. Only one car can fit in each spot, just like only one molecule can bind to each receptor. In this case, if the orexin cannot bind to the receptor, it won't activate it to promote wakefulness.

The use of orexin antagonists is contraindicated in patients with narcolepsy and should be used cautiously in patients taking CNS depressants or those patients with a history of depression or suicidal ideation. Side effects of the orexin antagonists include somnolence or fatigue, sleep paralysis, nightmares or abnormal dreams, and hypnagogic hallucinations (imagined sensations that feel real).

Refer to Table 19-5 for a summary of the sedatives and hypnotics.

Table 19-5 Sedatives and Hypnotics (Use Hypnotics Short-Term Only)

Generic Name	Trade Name	Dosage	Comments
Benzodiazepines			
temazepam	Restoril	7.5–30 mg PO at bedtime	Intermediate onset, duration
triazolam	Halcion	0.125–0.25 mg PO at bedtime	Can cause amnesia, hallucinations, bizarre behavior, rapid onset, and short duration
quazepam	Doral	PO 7.5–15 mg at bedtime	May reduce dose after 1–2 nights
Nonbenzodiazepines			
eszopiclone	Lunesta	PO 1–3 mg at bedtime	Rapid onset; not limited to short-term use
zolpidem	Ambien[a]	5–10 mg PO at bedtime	Rapid induction 30 min; short half-life (less than 3 h); CR not limited to short-term use

Generic Name	Trade Name	Dosage	Comments
	Ambien CR[a]	PO 6.25–12.5 mg at bedtime	
	Intermezzo	SL 1.75 or 3.5 mg one per night	For middle-of-the-night awakening with 4 h left before planned wake time
	Zolpimist	Nasal spray 5 mg at bedtime	Schedule IV
zaleplon	Sonata	PO 5–10 mg at bedtime	Rapid onset, very short half-life
Melatonin Receptor Agonist			
ramelteon	Rozerem	PO 5–10 mg within 30 min of bedtime	Not limited to short-term use; not a controlled substance
tasimelteon	Hetlioz	PO 20 mg at bedtime	Take at the same time each night
Orexin Antagonists			
suvorexant	Belsomra	PO 5–20 mg within 30 min of bedtime	Take with at least 7 h of sleep remaining schedule IV
lemborexant	Dayvigo	PO 5–10 mg immediately before bedtime	Take with at least 7 h of sleep remaining; Schedule IV
daridorexant	Quviviq	PO 25–50 mg immediately before bedtime	Take with at least 7 h of sleep remaining; Schedule IV

[a] Recent FDA warning suggests limiting dose in females to 5 mg regular release and 6.25 mg controlled release because of prolonged levels in blood and slower elimination than males.

Other benzodiazepines will be discussed in Chapter 20; the three included in this chart are specifically indicated for sleep.

Patient Education

Patients taking analgesics, sedatives, or hypnotics should be instructed regarding:

- Potential for physical and psychological dependence and tolerance with opioids, sedatives, and hypnotics
- Taking only limited doses for short periods of time, except to relieve pain in terminal illness (in terminal cases, analgesics should be given on a regular basis around the clock to prevent or control pain)
- Caution with interactions; not taking any medications (except under close medical supervision) that potentiate CNS depression (e.g., psychotropics, alcohol, muscle relaxants, antihistamines, antiemetics, cardiac medications, and antihypertensives)
- Serious potential side effects with prolonged use or overdose of opioids, sedatives, and hypnotics (e.g., oversedation; dizziness; headache; confusion; agitation; nausea; constipation; urinary retention; and potentially fatal respiratory depression, bradycardia, or hypotension)
- Tolerance with prolonged use, with increasingly larger doses required to achieve the same effect
- Potential for overdose of sedatives or hypnotics and **paradoxical** reactions with older adults (e.g., confusion, agitation, hallucinations, and hyperexcitability)
- Withdrawal after prolonged use of sedatives and hypnotics, possibly leading to rebound effects with nightmares, hallucinations, or insomnia
- Mental alertness and physical coordination impairment, causing accidents or falls
- Caution regarding OTC analgesic and sleep aid combinations and checking ingredients on the label; being aware of possible side effects with those containing aspirin (e.g., gastric distress or bleeding)
- Not discontinuing abruptly
- Proper storage and disposal of these medications

The website https://www.practicalpainmanagement.com/ is a very good resource that provides open access to clinical news, information, research, and education for evidence-based pain-management practices.

Case Study A

Analgesics

A patient is in the recovery room after just having undergone a right total hip replacement for severe arthritis. In addition to arthritis, the patient has a history of stomach/duodenal ulcers, high cholesterol, and gout.

1. The recovery room nurse will administer which category of medication *first* to relieve the patient's pain?
a. hypnotic
b. sedative
c. analgesic
d. anti-inflammatory

2. After administering an opioid analgesic, the nurse should observe the patient for which side effect?
a. constipation
b. respiratory depression
c. abdominal pain
d. hypoglycemia

3. The best method to assess the patient's response to the analgesic is to observe
a. her facial expression
b. her respiratory rate
c. the rating of her pain on a pain scale
d. the ability to open her eyes

4. Due to the patient's history, which nonopioid analgesic should be avoided??
a. NSAIDs
b. lidocaine patch
c. acetaminophen
d. muscle relaxants

5. The nurse administering an opioid will use extreme caution if the patient has a history of
a. arthritis
b. allergy to penicillin
c. COPD
d. Cataracts

Case Study B

Hypnotics

A patient has been experiencing insomnia for the past 6 weeks. At an annual physical, the patient asks their physician if Lunesta (eszopiclone), the medication in the television commercial, is an option. The patient's medical history includes mild cluster headaches that are relieved with acetaminophen. The patient works as a computer technician and spends most of their day seated in front of computer monitors. Usually when the patient comes home, they take a 1-h nap and then drink a coffee afterward so they can have energy to play with their young children. They generally shower before bedtime and read a book for 15–30 min before turning off the light. The patient states they generally take a long time to fall asleep and wake up four to five times each night.

1. The physician explains to the patient that hypnotic medications should not be used for extended amounts of time except under close medical supervision. What is the primary reason for this?
a. loss of functioning due to an inability to stay awake during the day
b. an increase in REM sleep as a withdrawal symptom
c. risk of cardiac arrest
d. physical and psychological dependence

2. Eszopiclone falls into which category of sedatives or hypnotics?
   a. nonbenzodiazepine
   b. benzodiazepine
   c. melatonic receptor agonist
   d. antihistamine

3. The physician informs the patient that before starting hypnotics, there are nonpharmacological ways to help with insomnia. Based on the patient's daily habits, what should they change to help promote healthy sleep?
   a. They should not read before bed.
   b. They should only shower in the morning.
   c. They should try to avoid daytime naps and caffeine intake late in the day.
   d. They should not change anything; nonpharmacological methods are not effective when used alone, but need to be combined with a hypnotic.

4. The physician warns the patient that when taking a hypnotic, they may develop tolerance. What does this mean?
   a. The body will release its own analgesia.
   b. A larger dose will be required over time to achieve the same effect.
   c. The patient will experience a lower pain threshold in the future.
   d. Relief from pain will be as a result of a suggestion without the actual administration of a medication.

5. The patient returns a month later stating the nonpharmacological methods have helped them fall asleep more easily but not stay asleep. What should the physician ask the patient about their sleep hygiene routine?
   a. Do you drink water before going to bed?
   b. Do you have vivid dreams that wake you up?
   c. Do you sleep with a humidifier near your bed?
   d. Do you drink alcohol before bedtime?

Chapter Review Quiz

Match the medication in the first column with the classification in the second column. Classifications may be used more than once.

Medication	Classification
1. ______ amitripytline	**a.** Antitussive
2. ______ Vicodin	**b.** Opioid antagonist
3. ______ Imitrex	**c.** Orexin antagonist
4. ______ Methadone	**d.** Tricyclic antidepressant (adjuvant)
5. ______ Belsomra	**e.** Opioid analgesic with acetaminophen
6. ______ Duragesic	**f.** Nonopioid analgesic (cannabinoid)
7. ______ dronabinol	**g.** Anticonvulsant (adjuvant analgesic)
8. ______ codeine	**h.** Antimigraine (triptan)
9. ______ Narcan	**i.** Opioid analgesic and narcotic withdrawal
10. ______ Tegretol	**j.** Transdermal analgesic for chronic pain

Choose the correct answer.

11. Which medication is used to treat opiate-induced respiratory depression?

a. butorphanol

b. naloxone

c. ethadone

d. oxycodone

12. Nonopioid analgesics like topical lidocaine (in some strengths), acetaminophen, and NSAIDs are commonly obtained by which method?

a. from a pharmacist

b. over the counter

c. with a prescription

d. from a mail-order company

13. What is a convenient aspect of topical lidocaine patches?

a. They dissolve in water, so they are safe to flush down the toilet.

b. They have a special adhesive that can be applied to both hairless and hairy areas.

c. They can be cut to the shape and size needed.

d. They do not expire.

14. Which group of medications would be useful in treating pain described as "sharp," "shooting," "shock-like," or "lightning-like"?

a. anticonvulsants like gabapentin

b. opioids like oxycodone

c. hypnotics like zolpidem

d. tricyclic antidepressants like amitriptyline

15. Which of the following is not true for ramelteon and drugs in the same class?

a. They activate the melatonin receptors.

b. They should be taken within 30 min of going to bed with a high-fat meal or snack.

c. They are contraindicated with fluvoxamine.

d. They are controlled substances.

Chapter 20

Psychotropic Medications, Alcohol, Drug Abuse, and Withdrawal Treatment

Key Terms and Concepts

Addiction
Antidepressant
Antipsychotic
Anxiolytics
Ataxia
Atypical antipsychotics
Bipolar disorder
Chemical dependency
Extrapyramidal
Heterocyclic
Monoamine oxidase inhibitors (MAOIs)
Neurotransmitters
Prodrug
Psychotropic
Racemic
Selective norepinephrine reuptake inhibitors (SNRIs)
Selective serotonin reuptake inhibitors (SSRIs)
Tardive dyskinesia
Tricyclics

Objectives

Upon completion of this chapter, the learner should be able to:

1. Categorize the most commonly used psychotropic medications according to the following classifications: central nervous system (CNS) stimulants for promoting wakefulness and treating attention-deficit hyperactivity disorder (ADHD), antidepressants, antimanic agents for bipolar disorders, anxiolytics, and antipsychotic medications and tranquilizers.
2. List the purposes, actions, side effects, interactions, and precautions and contraindications for psychotropic medications in common use.
3. Explain the treatment of alcohol use disorder.
4. Describe the effects of commonly used illegal drugs.
5. List the responsibilities of a health care professional in combating drug abuse.

Psychotropic refers to any substance that acts on the mind. Psychotropic medications are drugs that can exert a therapeutic effect on a person's mental processes, emotions, or behavior. Examples of other medications that affect mental functioning are anesthetics, analgesics, sedatives, and hypnotics.

Psychotropic medications can be classified according to the purpose of administration. The psychotropic therapeutic agents discussed in this chapter include the following:

- Central nervous system (CNS) stimulants; example: to promote wakefulness
- Agents to treat attention-deficit hyperactivity disorder (ADHD)
- Antidepressants
- Antimanic agents to treat bipolar disorder

- Anxiolytic agents to treat anxiety
- Antipsychotic agents to relieve symptoms of psychoses, which can include delusions, hallucinations, and excessive combativeness

Keep in mind that psychotropic medications are frequently prescribed concurrently with psychotherapy or professional counseling. A reliable resource for anyone experiencing mental health issues is the U.S. Department of Health and Human Services website (https://www.samhsa.gov/find-help/national-helpline) (also available by phone: 1-800-662-HELP).

Drugs used for other purposes can also have psychotropic effects that can be harmful. Therefore, this chapter will conclude with a discussion on substance abuse and treatment.

CNS Stimulants

CNS stimulant medications are given for the purpose of promoting CNS functioning. Drugs in this category include caffeine, amphetamine and methylphenidate preparations, derivatives of amphetamine and methylphenidate, and the wakefulness-promoting agents.

Caffeine

Fatigue and drowsiness are part of everyday life for millions of people. The only over-the-counter (OTC) drug proven safe and effective in helping fight fatigue and drowsiness is caffeine (at doses of 100–200 mg not more often than every 3–4 h), found in products like NoDoz and Vivarin. One prescription-only drug in this category, caffeine citrate (Cafcit), has been used in the treatment of neonatal sleep apnea to stimulate the newborn's CNS respiratory drive.

Prolonged high intake of caffeine in any form may produce tolerance, habituation, and psychological dependence. Physical signs of withdrawal such as headaches, irritation, nervousness, anxiety, and dizziness may occur upon abrupt discontinuation of any stimulant, caffeine included. Excessive consumption of caffeine (especially when taken with alcohol or other drugs) can lead to life-threatening irregular heartbeats, heart attacks, and seizures. A rising number of patients, many of them young students, are being treated in emergency departments for complications related to the consumption of highly caffeinated energy drinks, sometimes mixed with alcohol.

Because caffeine crosses the placenta and is also distributed into the milk of nursing persons, most clinicians recommend that those who are pregnant (because of a higher risk of miscarriage) or nursing avoid or limit their consumption of foods, beverages, and drugs containing caffeine, for example, OTC analgesics and decongestants. All sources of caffeine should be included when calculating your daily intake.

Amphetamine and Methylphenidate Preparations

Other CNS stimulant drugs include the controlled substances (Schedule II) amphetamine/dextroamphetamine (e.g., Adderall), methylphenidate (Ritalin), as well as their derivatives and other formulations, which are used to treat both attention-deficit hyperactivity disorder (ADHD) in children over 6 years of age and narcolepsy. Amphetamine and methylphenidate preparations are the first-line therapy for ADHD. Many derivatives of these two stimulants have been approved for similar uses. While they tend to be more expensive and less likely to be approved for first-line therapy, medications like dextroamphetamine (Dexedrine) and lisdexamphetamine (Vyvanse) can be used in cases where amphetamine and methylphenidate are ineffective. Ritalin is also occasionally used in the treatment of senile apathy and major depression refractory to other therapies. For ADHD, it is common practice for a patient to be on two stimulant preparations, with one being a long-acting delayed-release form taken in the morning and the other being an immediate-release formulation taken around midday.

A newer formulation of methylphenidate called Jornay PM is unique because it is a delayed-release capsule taken at night. It is the only stimulant intended for nighttime use and it functions to release methylphenidate into the body in the morning and throughout the next day. Daytrana is a transdermal system that contains methylphenidate in an adhesive matrix skin patch that is difficult to reapply once taken off. The patch is formulated in a way that makes it difficult to extract drug from the patch (abuse deterrent). Xelstrym is a newly approved patch formulation that works in a similar manner as Daytrana but delivers the active ingredient dextroamphetamine. Another drug that has a lower risk for abuse is Vyvanse (lisdexamphetamine), which is a prodrug that is converted to dextroamphetamine in the gastrointestinal (GI) tract and used to treat ADHD. A **prodrug** is a biologically inactive compound which is metabolized in the body to produce an active drug compound. Similarly, the newly approved combination of serdexmethylphenidate and dexmethylphenidate (Azstarys) is also a prodrug formulation. Like Daytrana and Vyvanse, many newer products are formulated to have lower potential for abuse than other formulations.

The use of amphetamines to reduce appetite in the treatment of obesity is not recommended because tolerance develops rapidly and physical and/or psychological dependence may develop within a few weeks. *These drugs have a high potential for abuse and should be used only under medical supervision for diagnosed medical disorders.* However, when these drugs are used appropriately, as ordered by a physician, abuse potential (including abuse of other substances) and dependence appear to be minimal.

Side effects of the controlled CNS stimulants can include:

Nervousness, insomnia, irritability

❗ Tachycardia, palpitations, hypertension, and cardiac arrhythmias

Dizziness, headache, and blurred vision

GI disturbances

A Food and Drug Administration (FDA) review of reports of serious cardiovascular adverse events in patients taking usual doses of ADHD products revealed reports of sudden death in patients with serious underlying heart conditions or defects and reports of stroke and heart attack in adults with certain risk factors. The FDA recommends that children, adolescents, and adults who are being considered for treatment with ADHD drug products work with their physician or other health care professionals to develop a treatment plan that includes a careful health history and evaluation of current status, particularly for cardiovascular conditions and mental health disorders (including an assessment for a family history of such conditions).

Cautions or contraindications for the CNS stimulants apply to:

- Treatment for obesity (never more than 3 to 6 weeks) without diet and exercise modifications (weight gain resumes after discontinuation of the medication)
- Anxiety or agitation
- History of drug dependence, alcohol use disorder, or eating disorders
- Hyperthyroidism
- Cardiovascular disorders
- Closed-angle glaucoma (not modafinil)
- Pregnant or nursing persons
- Abrupt withdrawal (depression results)
- Use with monoamine oxidase inhibitors (MAOIs) (may cause hypertensive crisis)

Caution must be used with sustained-release preparations differing in designations (CD, ER, LA, SR) and their respective dosing requirements (refer to Table 20-1).

Pediatric precautions: Prolonged administration of CNS stimulants to children with ADHD has been reported to cause at least a temporary suppression of normal weight and/or height patterns in some patients, and therefore close monitoring is required. Growth rebound has been observed after discontinuation, and attainment of normal adult weight and height does not appear to be compromised. Children should also be observed carefully for the development of tics while receiving these drugs.

There is some evidence that medication use only during school days may be tried in children with controlled ADHD (in those children whose symptoms precipitate primarily in the school setting), but only if no significant behavior or social difficulties are noted. Once controlled, dosage reduction or interruption ("drug holidays") may be possible during weekends, holidays, or vacations.

Wakefulness-Promoting Agents

Modafinil (Provigil) and armodafinil (Nuvigil) are psychostimulant medications approved for narcolepsy, sleep apnea, and shift-work sleep disorder (resulting from night shift work) in adults and adolescents (>16 years old). The potential for abuse and dependence is lower than that for the amphetamines and methylphenidate. These medications are not approved by the FDA for ADHD because of serious side effects that developed with the doses used in clinical trials. They have also not been demonstrated to promote weight loss.

Side effects of modafinil (Provigil) and armodafinil (Nuvigil) for approved indications are infrequent and include:

- Mild headache, dizziness, nausea, and anorexia
- Anxiety, depression, and mood changes
- Hypertension, palpitations, and tachyarrythmia

Cautions for the use of modafinil and armodafinil: Possible causes of fatigue and sleepiness should be determined before stimulant medicines are prescribed to increase wakefulness. Without adequate investigation, some common disorders, such as diabetes and sleep apnea, might go undiagnosed.

Reducing the necessary amount of restorative sleep for prolonged periods of time can result in mental health and physical conditions, especially neurological and cardiovascular effects.

Patient Education

Patients receiving the controlled CNS stimulants should be warned regarding (utilize the patient medication guide that is given out each time these products are dispensed):

- Potential side effects
- Potential for abuse and taking the medications only according to the physician's orders
- Taking the medication early in the day to reduce insomnia
- The fact that abrupt withdrawal may result in depression, irritability, fatigue, agitation, and disturbed sleep
- Watching for signs of tics, gastric disturbance, insomnia, weight loss, or nervousness in children receiving amphetamines and methylphenidate and reporting them to the physician
- Potential for dangerous cardiovascular side effects
- Not chewing or crushing sustained-release products unless instructed to do so by the pharmacist
- For parents and caregivers, the potential for abuse with stimulants and signs of abuse such as running out of the medication early, rapid weight loss, and unusual changes in behavior
- Necessity for regular sleep in sufficient amounts to restore mental and physiological functioning to an optimal level while taking modafinil

Selective Norepinephrine Reuptake Inhibitor (SNRI) for ADHD

Atomoxetine (Strattera) and viloxazine (Qelbree) are selective norepinephrine reuptake inhibitors (SNRIs) and are *nonstimulant, noncontrolled* drugs approved for the treatment of ADHD. Atomoxetine and viloxazine do not have a potential for abuse, cause less insomnia, have less effect on growth, and have been shown to be safe and effective in adolescents and children more than 6 years old and adults with ADHD. They have a longer onset to therapeutic benefit and reduced efficacy compared to the stimulants. SNRIs are generally used alone in therapy but are safe to take with stimulants while transitioning between drug classes.

Side effects of SNRIs include:

- ❗ Dry mouth, reduced appetite, and fatigue
- ❗ Nausea, vomiting, constipation, and dyspepsia
- ❗ Urinary hesitation or retention
- ❗ Increased risk of suicidal tendencies in children and adolescents (black box warning)

Cautions or contraindications for SNRIs apply to:

- Narrow-angle glaucoma
- Cerebrovascular, heart, or hepatic disease

Interactions of SNRIs occur with:

- Beta agonists, vasopressor agents, and quinidine
- Fluoxetine, paroxetine, venlafaxine, and MAOIs

Refer to Table 20-1 for a summary of the CNS stimulants and nonstimulant medications for ADHD.

Table 20-1 Central Nervous System Stimulants and Nonstimulant Medications

Generic Name	Trade Name	Dosage	Comments
Stimulants			
caffeine citrate	Cafcit	PO 20–25 mg/kg one time and then 5–10 mg/kg per day	For neonatal apnea
amphetamine	Evekeo/Evekeo ODT Adzenys XR-ODT	PO 2.5–40 mg daily (can divide doses for Evekeo formulations)	For ADHD, obesity (short term), narcolepsy
amphetamine mixtures (amphetamine salts) (amphetamine/ dextroamphetamine)	Adderall	PO 2.5–60 mg daily in one to three divided doses per day (4–6 h apart)	For narcolepsy, ADHD (>3 years old)
	Adderall XR	PO 5–60 mg daily	For ADHD (>6 years old)
	Mydayis	PO 12.5–50 mg daily	Extended release capsule approved for ages 18–55
dextroamphetamine	Zenzedi	PO 2.5–30 mg in one to three divided doses per day	IR tablet
	Dexedrine	PO 5–40 mg qAM	ER capsule
	ProCentra	PO 2.5–30 mg in one to three divided doses per day	5 mg/5 mL oral solution
	Xelstrym	9–18 mg daily (apply 2 h before needed effect)	Remove patch after 9 h
dextroamphetamine and serdexmethylphenidate	Azstarys	26.1/5.2 mg to 52.3/10.4 mg daily in the morning	first and only product containing dexmethylphenidate prodrug
lisdexamfetamine	Vyvanse	PO 10–70 mg qAM (starting dose is 30 mg)	For ADHD (>6 years old)
methylphenidate	Ritalin, Methylin	PO 2.5–20 mg two to three times per day ac	For narcolepsy, ADHD (>6 years old)
	Ritalin SR, Metadate ER	10–60 mg divided doses (8-h duration of action)	ER tabs, for ADHD, senile apathy, refractory depression
	Metadate CD, Ritalin LA	PO 10–60 mg qAM	ER (extended-release) caps for once-daily treatment of ADHD
	Concerta	PO 18–72 mg qAM	Tablet shell is excreted intact
	Daytrana Patch	10–30 mg daily to hip (apply 2 h before needed effect)	Remove patch after 9 h
	Jornay PM	PO 20–100 mg qPM	Unique—taken at night
	Quillivant XR	25 mg/5 mL oral suspension	Can make unique doses and small dose adjustment easily
	QuilliChew ER	PO 20–40 mg daily	Scored tablet that can be split
modafinil armodafinil	Provigil Nuvigil	PO 100–400 mg daily PO 150–250 mg daily	For narcolepsy, sleep apnea, and shift-work sleep disorder (>16 years old)

Generic Name	Trade Name	Dosage	Comments
Nonstimulant			
atomoxetine	Strattera	PO 10–100 mg one to two times per day	Noncontrolled, nonstimulant for ADHD (>6 years old)
viloxazine	Qelbree	PO 100–200 mg daily	Noncontrolled, nonstimulant for ADHD (>6 years old)
clonidine ER	Kapvay	PO 0.1–0.4 mg at bedtime	For ADHD
guanfacine guanfacine ER	Tenex Intuniv	PO 1 mg starting dose daily; max dose increases with age up to 7 mg per day	For ADHD

Antidepressants

Major depressive disorder (MDD) is a mental health disorder characterized by an all-encompassing low mood accompanied by low self-esteem and loss of interest or pleasure in typically enjoyable activities. MDD is a significant health problem that affects about 21 million American adults annually, which is about 8% of the U.S. population. MDD affects females more frequently than males (by about 10%).

The exact cause of depression is unknown, but it may result from a chemical imbalance in the brain. Chemicals in the brain, like dopamine, serotonin, and norepinephrine, are known as **neurotransmitters**. Neurotransmitters are substances that travel across the synapse (contact point between two neurons) to transmit messages between nerve cells. In depression, there may be a shortage of the neurotransmitters dopamine, serotonin, or norepinephrine.

PHOTO/Shutterstock.com

Antidepressant medications, sometimes called mood elevators, are used primarily to treat patients with various types of depression. The five categories in general use are the tricyclic antidepressants, the **monoamine oxidase inhibitors (MAOIs)**, the **selective serotonin reuptake inhibitors (SSRIs)**, the **selective norepinephrine reuptake inhibitors (SNRIs)**, and the heterocyclic antidepressants. Although symptoms may be relieved in the first month, it may take 4–8 weeks to experience the drug's full effects; it is generally advisable to counsel patients to continue antidepressant therapy for 6 to 12 months or indefinitely to prevent relapse.

The FDA has directed manufacturers of *all* antidepressants to include a black box warning that antidepressants increase the risk of suicidal thinking and behavior (particularly during the first few months of therapy) in short-term studies in children and adolescents with manic depressive disorder and other psychiatric disorders. Anyone considering the use of antidepressants for a child, adolescent, or young adult must balance this risk with the clinical need. Patients should be observed closely for behaviors associated with these drugs (e.g., anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, severe restlessness, hypomania, and mania) and communicate the same with the prescribing health care provider.

Tricyclics

Among the first antidepressants in clinical use, the mechanism of action of the **tricyclics** involves potentiation of norepinephrine and serotonin activity by blocking their reuptake. Remember, by blocking the reuptake or reabsorption of a neurotransmitter it will remain around longer to have its effect. Their pharmacology also includes strong *anticholinergic* activity that is responsible for many of the side effects experienced. Tricyclics can be lethal in overdose (cardiac conduction abnormalities or dysrhythmias).

The tricyclics have delayed onset of action, meaning their full effects of elevating the mood and increasing alertness may not be experienced for 2 to 4 weeks. They are frequently given at bedtime because they have a mild sedative effect. They should be used with caution (if at all) in older adults because of the strong sedative and anticholinergic properties of this drug class and the increased risk of falls. Tricyclics may be more effective than SSRIs in some cases of severe depression and are used as an adjunct in neuropathic pain control.

Side effects of the tricyclics, such as imipramine (Tofranil), are anticholinergic in action and can include:

- ❗ Dryness of the mouth
- Increased appetite and weight gain
- ❗ Drowsiness and dizziness
- ❗ Constipation and urinary retention, especially with benign prostatic hyperplasia (BPH)
- Sexual dysfunction
- ❗ Postural hypotension, cardiac arrhythmias, and palpitations
- ❗ Confusion, especially in older adults

Cautions or contraindications for tricyclics apply to:

Cardiac, renal, GI, and liver disorders
Older adults
Glaucoma
Obesity
Seizure disorder
Pregnancy and lactation
Concomitant use with MAOIs

Interactions of tricyclics occur with:

Certain antiarrhythmics and some quinolones (QT prolongation)
Clonidine (hypertensive crisis)
CNS drugs and alcohol
SSRIs (increase tricyclic blood levels)

Learning Hint

Compliance is a major concern for medications that do not exhibit immediate improvement of symptoms. Like tricyclics, many antidepressant medications take multiple weeks of adherent treatment to achieve the full effect. If patients are unaware of this, they may discontinue antidepressant medication after a few days, thinking it is not working. To help explain this to patients, think of it like a weight loss goal. When someone starts eating healthy and exercising more, they do not expect to experience results right after their workout or the morning after eating healthy food the previous day. Losing weight takes consistency and time to experience results, just like antidepressants need consistency and time to yield the full effect!

Monoamine Oxidase Inhibitors

The mechanism of antidepressant action of MAOIs involves increasing the concentrations of serotonin, norepinephrine, and dopamine in the neuronal synapse by inhibiting the MAO enzyme that degrades or breaks down these neurotransmitters, again allowing them to remain around longer to have their effects.

The MAOIs, for example, phenelzine (Nardil), are rarely used today because of potential serious side effects and numerous food, herbal, and drug interactions. They cannot be given until two weeks after tricyclics and other interacting drugs have been discontinued. These agents are typically reserved for refractory or atypical depression, depression associated with panic disorders or phobias, or for those patients who have proven long-term success with this treatment.

Side effects of MAO inhibitors are adrenergic in action and can include:

❗ Nervousness, agitation, and insomnia
❗ Hypertension or hypertensive crisis (can be fatal)
❗ Tachycardia, palpitations, and chest pain

Cautions or contraindications for MAOIs apply to:

Patients with cerebrovascular, heart, liver, and renal diseases
Children under 16 years of age

Pregnancy and lactation

Abrupt discontinuation (need to titrate down)

Interactions of the MAOIs with some drugs, foods, and herbal supplements can cause *hypertensive crisis*, manifested by severe headache, palpitations, sweating, chest pain, possible intracranial hemorrhage, and even death. Interactions may occur with:

Adrenergic drugs and levodopa

SSRIs and SNRIs (resulting in seizures, fever, hypertension, and confusion—serotonin syndrome)

CNS depressants (resulting in circulatory collapse)

Foods containing tyramine, tryptamine, or tryptophan, such as yogurt, sour cream, all cheeses, liver (especially chicken), pickled herring, figs, raisins, bananas, pineapple, avocados, broad beans (Chinese pea pods), meat tenderizers, alcoholic beverages (especially red wine and beer), and all fermented or aged foods (e.g., corned beef, salami, and pepperoni)

Emsam (selegiline) is a selective MAOI (type B) administered as a transdermal patch indicated for the treatment of MDD in adults. Transdermal administration allows for lower doses and direct absorption into the bloodstream, reducing the likelihood of a dietary tyramine–induced hypertensive crisis.

Selective Serotonin Reuptake Inhibitors

SSRIs are considered to be the first-line medications for the treatment of depression. They are preferred because of fewer side effects, greater safety in cases of overdose, and increased patient compliance.

The antidepressants in this category selectively block the reabsorption of the neurotransmitter serotonin, thus helping to restore the brain's chemical balance. Therapy may be required for several months or longer. Symptomatic relief may require one to four weeks. SSRIs do not significantly affect cognition in older adults. Fluoxetine and escitalopram (Lexapro) are the only antidepressants recommended for the treatment of MDD in adolescents (ages 12–17 years), and fluoxetine is also approved for children aged 8 years and older. Most SSRIs can also be used for anxiety disorders or obsessive compulsive disorder (OCD) when given at lower doses.

Side effects of the SSRIs may include:

Sexual dysfunction

❗ Nausea and other gastrointestinal (GI) effects (the most common side effects during the first two weeks of therapy, but often transient)

Anorexia and sweating

❗ Insomnia, anxiety, nervousness, tremor, drowsiness, fatigue, dizziness, and hyponatremia (low sodium levels)

Caution with SSRIs applies to patients with the following conditions:

Liver or renal impairment

Suicide prone

Diabetes

Bipolar disorders (may precipitate manic attacks)

Underweight

Eating disorders

Pregnancy and lactation

Abrupt discontinuation (taper down)

Interactions of SSRIs are possible with:

MAOIs (never take concurrently)

Amphetamines, most antidepressants, certain analgesics (fentanyl, tramadol), antiemetics (metoclopramide), antimigraines ("triptans"), antibiotics (linezolid), and OTC products (dextromethorphan, St. John's wort, tryptophan) (can result in serotonin syndrome—a potentially life-threatening reaction to excessive serotonin activity in the CNS)

Anticoagulants, antiplatelet drugs, NSAIDs, and aspirin (increased risk of bleeding complications)

Selective Norepinephrine Reuptake Inhibitors

SNRIs such as duloxetine (Cymbalta) and venlafaxine (Effexor) are antidepressants that inhibit the reuptake of both serotonin and norepinephrine. Some SNRIs are also effective in patients with chronic pain (neuropathic pain, fibromyalgia, and musculoskeletal pain). Desvenlafaxine (Pristiq), also an SNRI, is indicated for the treatment of MDD.

Heterocyclic Antidepressants

The second-generation **heterocyclic** antidepressants are comparable in efficacy to the first-generation tricyclic antidepressants, but have differing effects on dopamine, norepinephrine, and serotonin and distinctly different adverse effect profiles. Bupropion (Wellbutrin) is considered an *activating antidepressant* (like most SSRIs) and can be useful in cases of severe depression characterized by extreme fatigue, lethargy, and psychomotor retardation. An activating antidepressant will not make you drowsy or tired as a side effect. It is also useful in helping to reduce relapse rates in persons who are quitting smoking and those patients who experience sexual dysfunction with other antidepressants. Bupropion has a risk of seizures, which increases with higher doses.

Clinical Connection

Racemic Mixture of Drugs

Many medications are developed as racemic mixtures of drugs. **Racemic** drugs consist of the active form of the drug combined with an inactive or a less active form. The inactive form of the drug does not contribute to the desired therapeutic effects but to the side effects associated with the medication. This becomes a problem at higher doses, sometimes forcing the patient to discontinue the medication. To combat this side-effect problem, many drugs have been reformulated as purer forms containing only the active form of the drug or a greater percentage of the active form. This allows for prescribers to increase the dose without the severe side effects. One example of this is the SSRI escitalopram (Lexapro), which is a purer form of the older drug citalopram (Celexa). Whereas Escitalopram contains only the active form of the drug, citalopram (a racemic drug) contains a 50:50 mixture. In other words, 20 mg of escitalopram will give the same therapeutic benefits as 40 mg of citalopram, but with potentially fewer side effects. This strategy is used in other medications as well, but it should be noted that although this method is advantageous to therapy, it is more expensive to develop and produce the purer forms of drugs, which can sometimes limit availability for patients.

Mirtazapine (Remeron) is a *calming antidepressant* that can be useful in treating agitated depression, mixed anxiety and depression, and fibromyalgia. A common side effect of mitrazapine is weight gain, which can be helpful in patients with a poor appetite. Trazodone is highly sedating and is used in low doses as a hypnotic. It can be useful in higher doses in older adult patients for treating agitation secondary to dementia and treating activation side effects caused by the SSRIs. It is also commonly used in patients who are experiencing both insomnia and depression (at lower doses), as it is approved for both indications.

Side effects of heterocyclic antidepressants can include:

- ❗ Drowsiness—common (except bupropion)
- ❗ Insomnia, restlessness, agitation, and anxiety (with bupropion)
- ❗ Dry mouth, nausea, dizziness, and confusion
- Priapism (prolonged penile erection) or impotence (trazodone; discontinue the drug)
- ❗ Weight gain (mirtazapine, trazodone)

Interactions of heterocyclics occur with:

- Other CNS depressants, including alcohol—may potentiate sedation (mirtazapine, trazodone) or increase the risk of seizures (bupropion)
- MAOIs (never take concurrently)
- Food may decrease incidence of lightheadedness

Caution with heterocyclics applies to:

- Patients who are suicide prone
- Patients with anorexia and bulimia (bupropion)
- Seizure disorder (bupropion)
- Cardiac or liver disorders

Refer to Table 20-2 for a summary of the antidepressant agents.

Table 20-2 Antidepressants

Generic Name	Trade Name	Dosage	Comments
Tricyclics			
amitriptyline	(Elavil)[a]	PO 10–300 mg daily	All of these drugs interact with CNS drugs; give at bedtime
desipramine	Norpramin	PO 100–200 mg HS or q12h	Less sedation, anticholinergic SE, and orthostatic hypotension
doxepin	(Sinequan)[a]	PO 50–300 mg daily	Also used topically for eczema (Prudoxin)
imipramine	Tofranil	PO 75–300 mg daily	Also effective for enuresis
nortriptyline	Pamelor	PO 25–150 mg daily	Older adults and adolescent patients need lower dose

Generic Name	Trade Name	Dosage	Comments
protriptyline	Vivactil	PO 15–60 mg daily divided into two doses (spaced 6–8 h apart)	For adults and children over the age of 12 years
MAOIs			
isocarboxazid	Marplan	PO 20–60 mg daily in divided doses	All of these drugs interact with many foods and other drugs, resulting in serious reactions
phenelzine	Nardil	PO 45–90 mg daily in divided doses	
selegiline	Emsam	Transdermal patch applied daily 6 mg/24 h–12 mg/24 h	For depression in adults only
tranylcypromine	Parnate	PO 60 mg daily in divided doses	
SSRIs			
citalopram	Celexa	PO 10–40 mg daily	Doses >40 mg associated with QT prolongation
escitalopram	Lexapro	PO 5–20 mg daily	May be better tolerated than Celexa
fluoxetine	Prozac	PO 10–80 mg daily	Delayed response, long half-life; take in A.M.
paroxetine	Paxil	PO 10–60 mg daily	Older adults 1/2 dose; take in A.M.
	Paxil CR	PO 12.5–62.5 mg daily	Do not give with antacids
sertraline	Zoloft	PO 25–200 mg daily	Take in A.M.
vortioxetine	Trintellix	PO 10–20 mg daily	For depression in adults only
SNRIs			
desvenlafaxine	Pristiq	PO 50–400 mg daily	Do not chew or crush
duloxetine	Cymbalta	PO 20–60 mg daily	Also used for neuropathy
levomilnacipran	Fetzima	PO 40–120 mg daily (titrate with 2 days of 20 mg qd then increase to 40 mg qd)	For depression in adults only
milnacipran	Savella	Titrate PO to 50–100 mg bid	Only approved for fibromyalgia
venlafaxine	Effexor[a]	PO 75–375 mg divided doses	Take PC to lessen nausea
	Effexor-XR	PO 37.5–225 mg daily	Do not chew or crush; swallow whole
Heterocyclics			
bupropion	Wellbutrin	PO 100–150 mg two to three times per day	Take early in the day; space doses at least 6 h apart to minimize seizure risk
	Wellbutrin SR	PO 150–200 mg daily–two times per day	Space doses at least 8 h apart
	Wellbutrin XL	PO 150–400 mg	Give once daily in the A.M.

(*Continued*)

Table 20-2 Antidepressants (*Continued*)

Generic Name	Trade Name	Dosage	Comments
mirtazapine	Remeron	PO 15–45 mg daily	Take at bedtime; sedation is common
trazodone	Desyrel	PO 25–300 mg at bedtime for insomnia	Take PC to decrease dizziness and nausea; if drowsiness occurs, may give large portion of dose at bedtime
		PO 150–600 mg in divided doses for depression	

[a] This brand name is no longer marketed, but the name is still commonly used.

Antimanic Agents

Bipolar disorder, sometimes called manic depression, is a mental illness that is characterized by severe fluctuations in mood extremes (refer to Figure 20-1). Patients may experience high (mania) and low (depression) mood swings with a diminished capacity for daily functioning. The cause of bipolar disorder is most likely an imbalance in brain chemicals that affect mood. Without treatment, bipolar disorder is a debilitating condition that will not improve on its own.

Lithium

Lithium salts are approved for the treatment of mania and the treatment and prophylaxis of bipolar disorder. They prevent more manic episodes compared with depressive episodes. Lithium is the only mood stabilizer that has lowered the suicide rate in bipolar patients. A maintenance dose is established by monitoring blood levels. Serum levels are checked 7 days after starting or changing the lithium dose and every 6–12 months once a stable dose is established to maintain a level of 0.8–1.2 mEq/mL. Patients must be monitored and educated about signs of toxicity.

Image Point Fr/Shutterstock.com.

Figure 20-1 Bipolar disorder is often described as not being able to "settle" on one mood, oftentimes going from extremely happy to upset or depressed and back again frequently and rapidly.

Side effects of lithium can include:

- ❗ GI distress (usual initially and resolves—take medicine with meals)
- ❗ Cardiac arrhythmias and hypotension
- Thirst and polyuria (dehydration may cause acute toxicity)
- Weight gain
- ❗ Tremors (can be treated with propranolol)
- Thyroid conditions—hypothyroidism, goiter

Signs of lithium toxicity can include:

- ❗ Drowsiness, confusion, blurred vision, and photophobia
- ❗ Tremors, muscle weakness, seizures, coma, and cardiovascular collapse

Caution with lithium when given to patients with the following conditions:

- Seizure disorders and parkinsonism
- Cardiovascular and kidney disorders
- Older adults and patients in a severely weakened state
- Thyroid disease

Interactions of lithium occur with CNS drugs, most antidepressants, diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, and sodium salts.

The anticonvulsants valproate (Depakote, Depakene), lamotrigine (Lamictal), and carbamazepine (Tegretol) are also used for mood stabilization in bipolar illness.

Symbyax, a combination of the atypical antipsychotic olanzapine and the SSRI fluoxetine, is the first FDA-approved combination product for the depressive phase of bipolar disorder. In addition, the atypical antipsychotics aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone are approved to treat the manic phase of bipolar disorder. Lumateperone (Caplyta) is the newest drug approved to treat bipolar disorder and other mental health disorders such as schizophrenia. It can be taken alone, or with lithium or valproate. Refer to the discussion of these agents in this chapter for further details.

Refer to Table 20-3 for a summary of antimanic agents.

Table 20-3 Antimanic Agents

Generic Name	Trade Name	Dosage	Comments
lithium	Lithobid	900–1,800 mg divided doses	0.8–1.2 mEq/mL (desired serum level)
carbamazepine	Tegretol, Tegretol XR	PO 600–1,600 mg in divided doses	4–12 mcg/mL (desired serum level)
lamotrigine	Lamictal	Titrate up to PO 200 mg daily	May be more effective than lithium for preventing depressive episodes
valproate	Depakote DR	PO 750–2,500 mg per day (divided doses)	50–125 mcg/mL (desired serum level)
	Depakene		IR capsule, liquid
	Depakote ER	PO 250–1,000 mg per day	For migraine prophylaxis

(*Continued*)

Table 20-3 Antimanic Agents (*Continued*)

Generic Name	Trade Name	Dosage	Comments
olanzapine/fluoxetine	Symbyax	PO qPM (various strengths)	For bipolar depression
lumateperone	Caplypta	42 mg PO daily	For bipolar depression

Anxiolytics

Anxiety disorders are present in over 40% of individuals in the United States, accounting for 19% of the U.S. population, making them the most common mental health disorder. Anxiety is the body's natural response to real or perceived danger. This natural response becomes a disorder when it is excessive and difficult to control and when it leads to significant distress and impairment. Types of anxiety disorders include social anxiety, posttraumatic stress disorder, panic attacks, and obsessive–compulsive behavior.

Benzodiazepines

Benzodiazepines (BDZs) are sometimes referred to as **anxiolytics** or minor tranquilizers. They are useful for the short-term treatment of (1) anxiety disorders, (2) some psychosomatic disorders and insomnia, and (3) alcohol withdrawal. BDZs, such as diazepam (Valium), are also used as muscle relaxants, as anticonvulsants, in pre-procedural testing, and preoperatively for sedation induction. Clonazepam (Klonopin), used primarily in the management of seizures, is also used in the treatment of panic disorder.

Anxiolytic BDZs, when given in small doses, can reduce anxiety and promote relaxation without causing sedation. Larger doses are sometimes prescribed at bedtime for their sedative effect. The role of BDZs in treating anxiety disorders is providing acute relief of anxiety symptoms while waiting for long-term treatment (e.g., SSRI or SNRI antidepressants) to take effect. BDZs do not treat the underlying cause of anxiety (abnormality of neurotransmitters), but rather only mask the symptoms.

fizkes/Shutterstock.com.

Learning Hint

Although BDZs are not intended for long-term use, you may review a patient medication record with a long history of BDZ use. This is because BDZs are intended to be used PRN when prescribed long term. The patient should be on another "controller medication" such as an SSRI (at low doses), or hydroxyzine. Think of it like chronic pain therapy, where it is common for a patient to take a scheduled ER formulation to control pain while also taking an IR formulation for breakthrough pain. In the case of anxiety disorders, the BDZs are used to treat breakthrough anxiety or panic attacks. Many times, patients do not take their BDZs PRN as prescribed, and this results in the potential for dependence and abuse. Be aware of this when counseling patients on these drugs.

Minor tranquilizers should not be taken for prolonged periods of time because *tolerance and physical and psychological dependence may develop*. Alprazolam (Xanax) is one of the most abused BDZs because of its quick onset of action, which leads to euphoria. All BDZs are classified as Schedule IV controlled substances. *Sudden withdrawal (missed doses/discontinuation) after prolonged use may result in seizures, agitation, psychosis, insomnia, and gastric distress.*

BDZs with a long half-life, such as clorazepate (Tranxene) and diazepam, should be avoided in older adults. Oxazepam (Serax), temazepam (Restoril), and lorazepam (Ativan) have medium to short half-lives and inactive metabolites and are less prone to accumulation in older adult patients and those with liver disease.

Side effects of the BDZs may include:

❗ Depression, hallucinations, confusion, agitation, bizarre behavior, and amnesia
❗ Drowsiness, lethargy, and headache
❗ **Ataxia** and tremor
❗ Increased risk of falls in older patients by ~50%
Rash and itching
❗ Sensitivity to sunlight

Cautions or contraindications for BDZs apply to:

Depression
Suicidal tendencies; history of substance abuse
Depressed vital signs
Pulmonary disease and respiratory depression
Pregnancy and lactation
Children
Liver and kidney dysfunction
Persons operating machinery

Interactions of BDZs with potentiation of effect may occur with:

CNS depressants (e.g., analgesics, anesthetics, sedative hypnotics, other muscle relaxants, antihistamines, and alcohol); *Note*: potentially lethal overdose when BDZs are mixed with alcohol or opioids

Antiretroviral protease inhibitors, macrolides (erythromycin), azole antifungals (ketoconazole, itraconazole), oral contraceptives, and calcium channel blockers (diltiazem, verapamil) all reduce the elimination of most BDZs, leading to increased and excessive sedation or impaired psychomotor function

Phenytoin (potentiation of phenytoin by raising serum concentration)

Grapefruit juice can potentiate the effects of orally administered alprazolam, midazolam, and diazepam (should not be taken concurrently)

Other Anxiolytics

Other anxiolytics, not related to the BDZs, include buspirone (Buspar) and hydroxyzine (Vistaril). Unlike the BDZs, buspirone has no anticonvulsant or muscle relaxant activity, does not substantially impair psychomotor function, and has little sedative effect. It is indicated for the treatment of generalized anxiety disorder but not other anxiety disorders; it does not have activity against depression. Limited evidence suggests that whereas buspirone may be more effective for cognitive and interpersonal problems, including anger and hostility associated with anxiety, the BDZs may be more effective for somatic symptoms of anxiety. As mentioned earlier, SSRIs and SNRIs can be used at lower doses to treat anxiety.

Buspirone has a slower onset of action than most anxiolytics (two to four weeks for optimum effect). Therefore, it is ineffective on a PRN basis. It has little potential for tolerance or dependence and has been used without unusual adverse effects or decreased efficiency for as long as a year.

Side effects of midazolam can include:

❗ *Depressed respiration* with large doses, especially in older adults and those with COPD (chronic obstructive pulmonary disease)

Paradoxical reactions (agitation or involuntary movements) occasionally

Nausea and vomiting occasionally

Cautions with midazolam:

Watch for apnea, hypoxia, and/or cardiac arrest

Respiratory status should be monitored continuously during parenteral use

Facilities and equipment for respiratory and cardiovascular support should be readily available; vital signs should be monitored carefully for changes in blood pressure or decrease in heart rate

Patients with electrolyte imbalance, renal impairment, and congestive heart failure and children are at increased risk of complications

Contraindicated in pregnancy and those with acute narrow-angle glaucoma

Interactions of midazolam, which can potentiate the possibility of respiratory depression, occur with:

Cimetidine (Tagamet)

Same medications listed under BDZs

Clinical Connection

Midazolam (Versed) is a potent BDZ. It can be used preoperatively to relieve anxiety and provide sedation for general anesthesia, or in combination with an opioid such as fentanyl for painful procedures. Because of its more rapid onset of sedative effects and more pronounced amnesic effects during the first hour following administration, it is considered the drug of choice for short surgical procedures. Midazolam is usually administered IV, and the duration of amnesia is about 1 h. This potent sedative requires individualized dosage with adjustment for age, weight, clinical condition, and procedure. This means that extra care must be taken when selecting the correct dose for a patient.

Side effects of buspirone (fewer and less severe) may include:

Dizziness, drowsiness, and headache
GI effects (e.g., nausea)

Caution with buspirone applies to renal and hepatic impairment.

Another short-term anxiolytic, chemically different from the BDZs, is hydroxyzine (Vistaril). It is an antihistamine (H_1-blocker) structurally related to meclizine (Antivert). Hydroxyzine is also used IM as a pre- and postoperative antiemetic and sedative.

Side effects of hydroxyzine, generally anticholinergic in nature, may include:

❗ Drowsiness, ataxia, and dizziness
Urinary retention and mydriasis

Caution with hydroxyzine applies to:

GI, hepatic, respiratory, and urinary disorders
Closed-angle glaucoma
Older adults
Pregnancy (especially first trimester)

Refer to Table 20-4 for a summary of antianxiety medications.

Table 20-4 Antianxiety Medications (Anxiolytics)

Generic Name	Trade Name	Dosage	Comments
Benzodiazepines (Short-Term Use Only)			
alprazolam	Xanax	PO 0.125–0.5 mg bid–tid	Abrupt withdrawal may cause severe side effects; one of the most abused BDZs
	Xanax XR	PO 0.5–6 mg qAM	For panic disorder
chlordiazepoxide	Librium[a]	PO 5–25 mg tid or four times per day	Larger doses needed for ethanol withdrawal
clorazepate	Tranxene	PO 7.5–60 mg daily in divided doses	If used in older adult patients, no more than 15 mg daily
clonazepam	Klonopin	0.5–2 mg daily or in divided doses	
diazepam	Valium	PO 2–10 mg tid, IV	Do not mix in syringe with other medications; also used as a muscle relaxant or IV in status epilepticus
	Diastat	R 0.2 mg/kg	R for refractory seizures

(*Continued*)

Table 20-4 Antianxiety Medications (Anxiolytics) (*Continued*)

Generic Name	Trade Name	Dosage	Comments
lorazepam	Ativan	PO, IM, or IV 2–3 mg daily in divided doses	For older adults who are agitated
midazolam	Versed[a]	PO, IM, or IV dose varies with usage	Used preoperatively for short-term procedures
oxazepam	Serax[a]	PO 10–15 mg tid or four times per day	For older adults who are agitated
Other Anxiolytics			
buspirone	Buspar	PO 15–60 mg daily in divided doses	Slow onset of action; may be used long term Available in scored breakable tablets that can be broken for divided doses
hydroxyzine	Vistaril	PO 25–100 mg four times per day or 25–100 mg deep IM	Also used as an antiemetic and antipruritic or preoperatively

[a] This brand name is no longer marketed, but the name is still commonly used.

Antipsychotic Medications/Major Tranquilizers

Antipsychotic medications, or major tranquilizers, are sometimes called neuroleptics and consist of the traditional or *typical* (first-generation) and the newer or *atypical* (second-generation) agents. They are useful in relieving symptoms of psychoses, including delusion, hallucinations, agitation, and combativeness associated with conditions such as schizophrenia.

Most of the typical antipsychotics in use today are classified chemically as phenothiazines; for example, chlorpromazine (Thorazine) and butyrophenone derivatives such as haloperidol (Haldol). Dosage can be regulated to modify disturbed behavior and relieve severe anxiety in many cases without profound impairment of consciousness. These agents work primarily by blocking dopamine receptors, which accounts for their antiemetic effects, but their use also results in unbalanced cholinergic activity, which causes frequent **extrapyramidal** side effects (EPS), including tardive dyskinesia (TD). The extrapyramidal system controls equilibrium and muscle tone, so EPS can include muscle rigidity; tremors; difficulty walking; and involuntary, repetitive, and purposeless body movements called **tardive dyskinesia (TD)**. Despite their side effects, typical antipsychotics are still commonly used in the acute hospital setting because they are the only medications in this class available for IV administration.

The other class of antipsychotics, the **atypical antipsychotics** (for example, risperidone) are chemically different from the phenothiazines, blocking serotonin and transiently blocking dopamine receptors. This mechanism results in less potential for adverse effects, especially EPS and TD. The direct antagonism at the serotonin receptor may account for the weight gain commonly experienced with atypical agents.

Although helpful in treating behavioral and psychological symptoms of dementia, typical and atypical antipsychotic drugs are *not* FDA-approved (black box warning) for the treatment of older adult patients with dementia-related psychosis. Cerebrovascular adverse events (strokes, transient ischemic attacks, and cerebrovascular accidents), including fatalities (because of heart failure, sudden death, and infections), have been reported in older adults with dementia-related psychosis (Alzheimer's, vascular and mixed) being treated with antipsychotics.

Because there is no FDA-approved medication for the treatment of dementia-related psychosis, other management options (ruling out other causes, behavioral or environmental modifications, recreational activities, etc.) should be considered by health care providers. If antipsychotics must be utilized for dementia-related behaviors, they should be used at the lowest effective dose for the shortest duration necessary with appropriate documentation and justification of need.

Side effects of typical antipsychotics differ based upon the potency of the agent. Low-potency agents, including chlorpromazine and thioridazine, are more likely to produce sedation, hypotension, and anticholinergic effects. The remaining typical high-potency agents, including haloperidol, fluphenazine, and trifluoroperazine, are more likely to produce EPS.

Side effects of all antipsychotics may include:

Postural hypotension, tachycardia, bradycardia, and vertigo

❗ Anticholinergic effects: dry mouth, constipation, urinary retention, blurred vision, fever, confusion, restlessness, agitation, and headache

Jaundice, rash, photosensitivity, or hypersensitivity reactions

Metabolic effects (increased risk of hyperglycemia, insulin resistance, diabetes, weight gain, and elevated cholesterol) with the atypicals

Extrapyramidal side effects, severe CNS adverse effects, include:

❗ Parkinsonian symptoms, for example, tremors, drooling, dysphagia (more common in older adults)

TD (involuntary and maybe irreversible, abnormal orofacial movements such as tics—more common in older adults, especially females)

Dystonic reactions (spasms or abnormal muscle tone of the head, neck, or tongue—more frequent in children)

Akathisia (uncontrollable motor restlessness—more common in children)

Note

Tardive dyskinesia may become permanent and irreversible, and no treatment has been shown to be uniformly effective. Therefore, the best treatment is prevention. Patients receiving antipsychotic medication should be assessed for TD at the start of treatment and at least every six months thereafter with the Abnormal Involuntary Movement Scale (AIMS) (refer to Figures 20-2 and 20-3) or Dyskinesia Identification System: Condensed User Scale (DISCUS) available from https://www.medicalalgorithms.com/discus and other websites. Dosage should not be terminated abruptly in those receiving high doses for prolonged periods of time.

Cautions or contraindications for antipsychotics apply to:

Seizure disorders

Parkinsonian syndrome

Cerebrovascular disease

Severe depression

Pregnancy

Blood dyscrasias

Older adults and children

Hepatic, cardiovascular, and renal diseases

Prostatic hyperplasia and diabetes

INSTRUCTIONS: Complete Examination Procedure (reverse side) before making ratings.

Code: 0 = None, 1 = Minimal, may be extreme normal, 2 = Mild, 3 = Moderate, 4 = Severe

		(CIRCLE ONE)
FACIAL AND ORAL MOVEMENTS:	**1. Muscles of Facial Expression** e.g., movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing	0 1 2 3 4
	2. Lips and Perioral Areas e.g., puckering, pouting, smacking	0 1 2 3 4
	3. Jaw e.g., biting, clenching, mouth opening, lateral movement	0 1 2 3 4
	4. Tongue Rate only increase in movement both in and out of mouth, NOT inability to sustain movement	0 1 2 3 4
EXTREMITY MOVEMENTS:	**5. Upper (arms, wrists, hands, fingers)** Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous), athetoid movements (i.e., slow, irregular, complex, serpentine). Do NOT include tremor (i.e., repetitive, regular, rhythmic)	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4
TRUNK MOVEMENTS:	**7. Neck, shoulder, hips** e.g., rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4
GLOBAL JUDGEMENTS:	**8. Severity of abnormal movements**	0 1 2 3 4
	9. Incapacitation due to abnormal movements	0 1 2 3 4
	10. Patient's awareness of abnormal movements Rate only patient's report	No awareness 0 Aware, no distress 1 Aware, mild distress 2 Aware, moderate distress 3 Aware, severe distress 4
		No = 0 Yes = 1
DENTAL STATUS:	**11. Current problems with teeth and/or dentures**	No = 0 Yes = 1
	12. Does patient usually wear dentures?	

It is always preferable to perform the entire AIMS Examination. This establishes consistent testing conditions and allows test results to be compared. Nonambulatory residents may be observed informally for abnormal involuntary movements while in bed or in a wheelchair. Uncooperative residents should be observed during normal activities.

You must check one of these boxes: ☐ Full examination conducted and scored
☐ Scores from informal observations—Resident was:
☐ Not ambulatory—observed in ☐ bed ☐ wheelchair
☐ Not cooperative

RATER	DATE:	PATIENT	Resident #

Figure 20-2 Abnormal Involuntary Movement Scale (AIMS). This test, or a comparable one, is performed every three to six months with all patients receiving antipsychotic medication to identify any signs of tardive dyskinesia.

AIMS EXAMINATION PROCEDURE

Either before or after completing the examination procedure observe the patient unobtrusively, at rest (e.g., in waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask patient whether there is anything in his/her mouth (i.e., gum, candy, etc.) and if there is, to remove it.
2. Ask patient about the current condition of his/her teeth. Ask patient if he/she wears dentures. Do teeth or dentures bother patient now?
3. Ask patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position.)
5. Ask patient to sit with hands hanging unsupported. If male, between legs, if female and wearing a dress, hanging over knees. (Observe hands and other body areas.)
6. Ask patient to open mouth. (Observe tongue at rest within mouth.) Do this twice.
7. Ask patient to protrude the tongue. (Observe abnormalities of tongue movement.)

◆ 8. Ask patient to tap thumb, with each finger, as rapidly as possible for 10–15 seconds; separately with right hand, then with left hand. (Observe facial and leg movements.)

9. Flex and extend patient's left and right arms (one at a time). (Note any rigidity and rate on DOTES.)
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included.)

◆ 11. Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth.)

◆ 12. Have patient walk a few paces, turn, and walk back to the chair. (Observe hands and gait.) Do this twice.

◆ Activated movement, some practitioners score these movements differently.

INTERPRETATION OF THE AIMS SCORE

- Individuals with no single score exceeding 1 are at very low risk of having a movement disorder.
- A score of 2 in only one of the seven body areas is borderline and the patient should be monitored closely.
- A patient with score of 2 in two or more of the seven body areas should be referred for a complete neurological examination.
- A score of 3 or 4 in only one body area warrants referring the patient for a complete neurological examination.

Figure 20-3 Abnormal Involuntary Movement Scale (AIMS). Examination procedure form.

Clinical Connection

Treatment of parkinsonian symptoms includes simultaneous administration of an anticholinergic antiparkinsonian agent, for example, Artane or Cogentin. Using these drugs will not prevent extrapyramidal symptoms or alleviate symptoms of TD. These parkinsonian symptoms usually appear early in the therapy and usually subside rapidly if/when the antipsychotic drug is discontinued. Trihexyphenidyl (Artane), benztropine (Cogentin), and diphenhydramine (Benadryl) are used to treat dystonic reactions and can allow a patient to take antipsychotic medications without having parkinsonian side effects.

Interactions of the antipsychotics may include:

Potentiation with CNS depressants, anticholinergics, and antihypertensives

Drugs that prolong the QT interval

Dopamine antagonists (metoclopramide or promethazine), which increase the risk of TD and EPS

Antagonism with anticonvulsants (seizure activity may increase)

Refer to Table 20-5 for a summary of the antipsychotic medications. Refer to Figure 20-4 for a summary of the psychotropic drugs.

Table 20-5 Antipsychotic Medications/Major Tranquilizers

Generic Name	Trade Name	Dosage[a]	Comments
Typical (*These drugs frequently cause EPS with long-term use. Monitor closely.*)			
Phenothiazines			
chlorpromazine	Thorazine[b]	PO 30–800 mg one to four doses daily, also deep IM, or IV	Primarily for agitation; also for nausea and vomiting and severe behavior problems
fluphenazine	Prolixin[b]	IM, PO 0.5–40 mg daily in divided doses	For older adults, reduce dose to 1/2 or 1/4
perphenazine	Trilafon[b]	PO 4–64 mg daily in divided doses	For psychosis, nausea, and vomiting in adults
prochlorperazine	Compazine[b] Compro	PO, IM, or IV 5–10 mg PR 25 mg bid	For agitation; primarily for nausea and vomiting in adults
thioridazine	Mellaril[b]	PO 50–800 mg daily divided two to four times per day	For psychoneurosis, agitation, or combativeness
trifluoperazine	Stelazine[b]	PO 1–20 mg bid	For schizophrenia and short term for nonpsychotic disorders
Butyrophenone			
haloperidol	Haldol	PO, IV 0.5–30 mg daily divided two to three times	For agitation, especially with schizophrenia and delusions in older adults
	Haldol decanoate IM	IM 50–300 mg q4wk	

Generic Name	Trade Name	Dosage[a]	Comments
Atypical (Second Generation)			
aripiprazole	Abilify	PO 2–30 mg daily IM 9.75 mg (for agitation)	For schizophrenia; adjunct treatment for depression
	Abilify Maintena	400 mg IM monthly	For schizophrenia maintenance
asenapine	Saphris	PO 2.5–10 mg q12h	For schizophrenia and bipolar disorder
cariprazine	Vraylar	PO 1.5–6 mg daily	Normally titrated starting with 1.5 mg for 1 day then increasing to 3 mg on day 2
clozapine	Clozaril Fazaclo ODT	PO 12.5–900 mg (divided doses)	Monitor WBC, neutrophil count; agranulocytosis risk
olanzapine	Zyprexa	PO 5–20 mg daily	Reduce dose by ½ for older adults
	Zyprexa Zydis	IM 10 mg (maximum dose 30 mg per day)	For acute agitation Orally disintegrating tablet
paliperidone	Invega	PO 3–12 mg once daily	For schizophrenia; do not crush
	Invega Sustenna	IM 234 mg day one, 156 mg in one week, and then 117 mg monthly	
quetiapine	Seroquel	PO 50–800 mg daily (divided doses)	Monitor for orthostatic hypotension
	Seroquel XR		Also for depression associated with bipolar
risperidone	Risperdal	PO 1–4 mg bid	Reduce dose by ½ for older adults
	Risperdal Consta	IM 25–50 mg q2wk	For schizophrenia or adjunct therapy for bipolar disorder
ziprasidone	Geodon	PO 20–80 mg bid with food	Greater risk of cardiac disorders

[a] Varies with condition (divided doses).

[b] This brand name is no longer marketed, but the name is still commonly used.

There is no "ideal" antipsychotic medication. Both conventional and atypical antipsychotic medications are associated with significant adverse drug reactions. However, research indicates a chemical component in many forms of mental illness. By altering abnormal levels of certain chemicals in the brain, such as serotonin, norepinephrine, or dopamine, many patients with mental or emotional illness have been helped. Psychiatric hospitalization has decreased since the advent of antipsychotic medications.

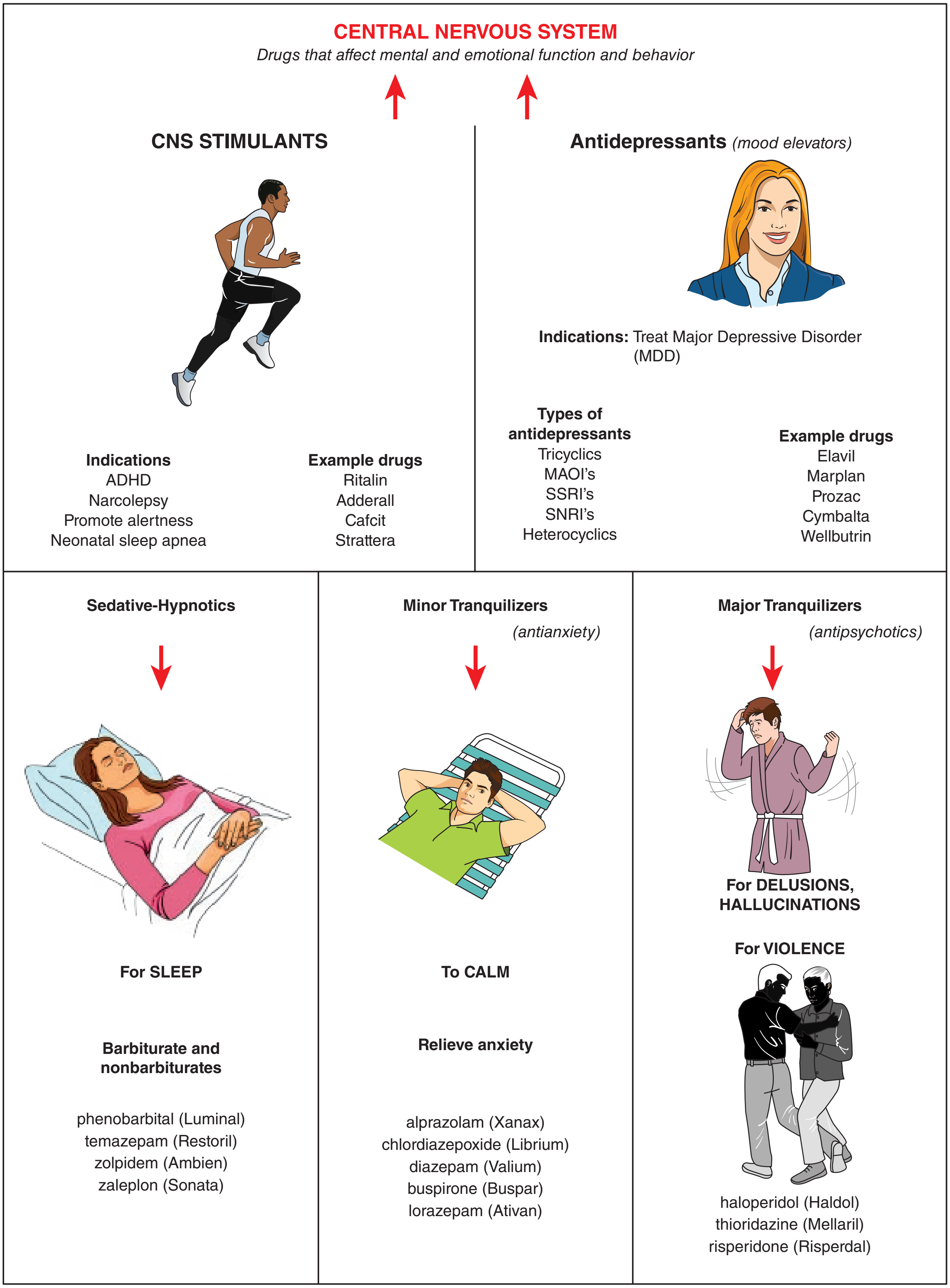

CENTRAL NERVOUS SYSTEM
Drugs that affect mental and emotional function and behavior
CNS STIMULANTS
Indications
ADHD
Narcolepsy
Promote alertness
Neonatal sleep apnea
Example drugs
Ritalin
Adderall
Cafcit
Strattera
Antidepressants (mood elevators)
Indications: Treat Major Depressive Disorder (MDD)
Types of antidepressants
Tricyclics
MAOI's
SSRI's
SNRI's
Heterocyclics
Example drugs
Elavil
Marplan
Prozac
Cymbalta
Wellbutrin
Sedative-Hypnotics
For SLEEP
Barbiturate and nonbarbiturates
phenobarbital (Luminal)
temazepam (Restoril)
zolpidem (Ambien)
zaleplon (Sonata)
Minor Tranquilizers
(antianxiety)
To CALM
Relieve anxiety
alprazolam (Xanax)
chlordiazepoxide (Librium)
diazepam (Valium)
buspirone (Buspar)
lorazepam (Ativan)
Major Tranquilizers
(antipsychotics)
For DELUSIONS, HALLUCINATIONS
For VIOLENCE
haloperidol (Haldol)
thioridazine (Mellaril)
risperidone (Risperdal)

Figure 20-4 Summary of psychotropic drugs.

Patient Education

Patients taking antipsychotic medications should be instructed regarding (utilize patient medication guides where available):

The importance of being compliant with medication and nonmedication therapy

Potential for psychological and/or physical dependence with prolonged use

Caution in taking the medication only in prescribed dosage and for a limited period of time under medical supervision to reduce the possibility of serious side effects from overdose or prolonged use

Reporting adverse side effects to the physician at once (e.g., dizziness, blurred vision, nervousness, palpitations and other cardiac symptoms, urinary retention, GI symptoms, adverse mental changes, and EPS)

Avoiding chemical abuse (e.g., alcohol, nicotine, and drugs) and obtaining professional treatment when these conditions exist

Possible severe withdrawal reactions (e.g., seizures) after prolonged use of psychotropic medications (withdrawal should never be abrupt, and medical supervision is indicated for prolonged administration of any of the psychotropic drugs)

Caution with interactions; *not* taking any other medications (except under close medical supervision) that can potentiate CNS depression (e.g., analgesics, alcohol, muscle relaxants, antihistamines, antiemetics, cardiac medications, or antihypertensives)

Not taking grapefruit juice with the BDZs, especially alprazolam and diazepam

Older adult patients are more at risk for the side effects mentioned earlier because of slowed metabolism and cardiovascular, kidney, liver, and visual impairment, and they should be issued the following cautions:

The need to rise slowly because of the potential for hypotension.

The need to avoid operating machinery or driving while taking these drugs until you know how they affect you. Report to the physician immediately any side effects, especially dizziness, confusion, sleep disturbances, or weakness.

The need to avoid taking any OTC drugs or herbal supplements without medical supervision.

The need to tell the prescribing physician about all other medicines you are taking, including eye drops.

Substance Abuse

Drug abuse can be defined as the use of a drug for other than therapeutic purposes. According to American Addiction Centers, an estimated 46.8 million individuals ages 12 and older in the United States battled a substance use disorder in 2023, accounting for nearly 17% of the population.

Drug **addiction** consists of the combination of all four of the following phenomena: tolerance, psychological dependence, physical dependence, and withdrawal syndrome with physiological effects. Habituation consists of psychological dependence only. **Chemical dependency** is the term used to describe a condition in which alcohol or drugs affect normal functioning and have taken control of an individual's life despite the problems related to their use.

Alcohol

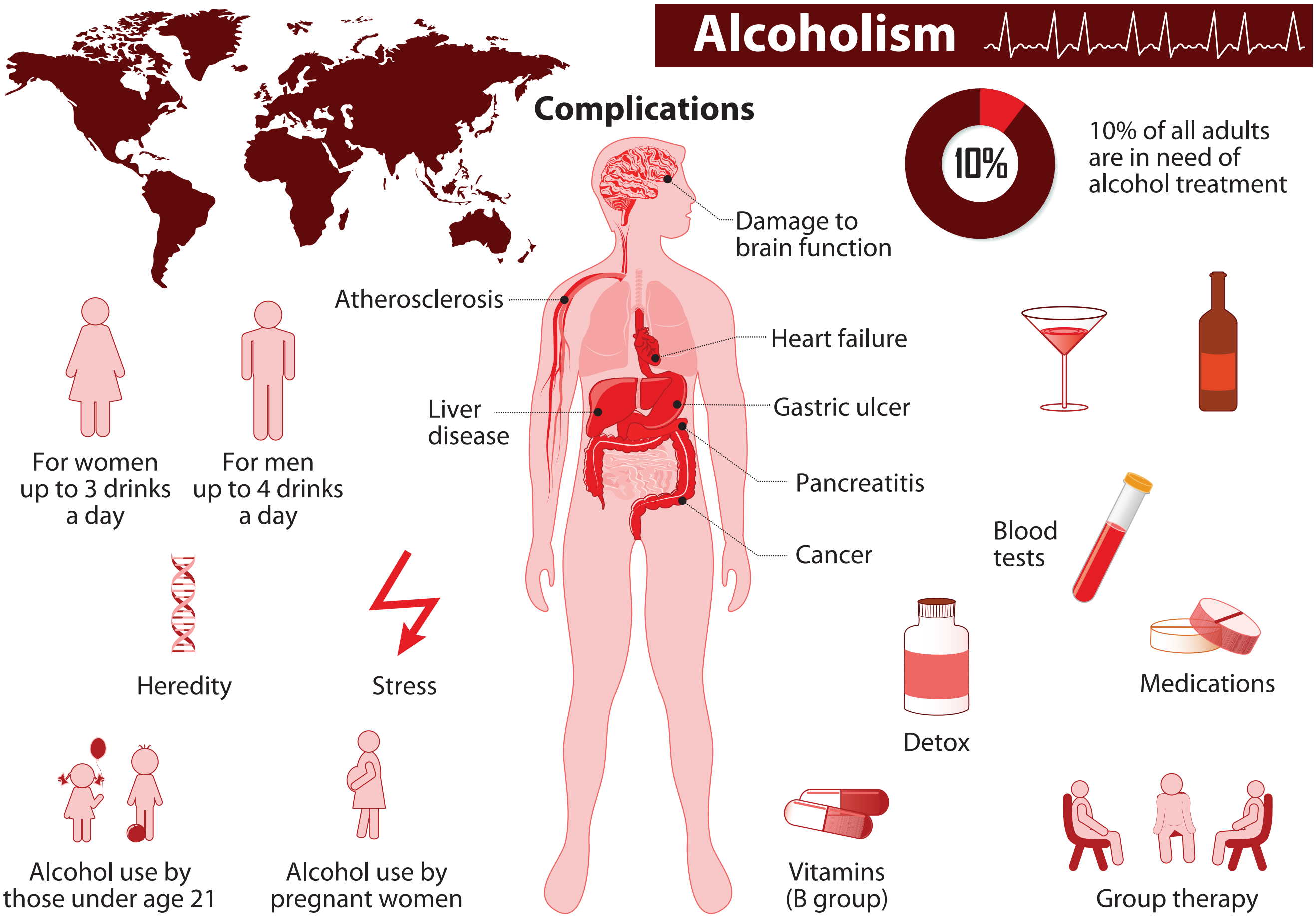
Alcohol (ethyl alcohol, ethanol) can be classified as a psychotropic drug and a CNS depressant. According to the CDC, it is the number one drug problem in the United States, responsible for about 178,000 deaths each year during 2020–2021, or 488 deaths per day. This was a 29% increase from 2016–2017, when there were an estimated 138,000 deaths per year, and indicates a growing problem. It is directly responsible for more than half of traffic accidents (one-third of all U.S. traffic fatalities). Alcohol is the most commonly abused drug among American teenagers.

Alcohol is a fast-acting depressant, pharmacologically similar to ether. The body reacts to alcohol with excitement, sedation, and finally anesthesia. Large amounts of alcohol can result in alcoholic stupor, cerebral edema, and depressed respiration.

Alcohol is rapidly absorbed from the GI tract into the bloodstream. Alcohol depresses primitive areas of the cortex first and then decreases control over judgment, memory, and other intellectual and emotional functioning. Within a few hours, motor areas are affected, producing unsteady gait, slurred speech, and uncoordinated movements. Prolonged use can cause permanent CNS damage and result in peripheral neuritis, convulsive disorders, Wernicke's syndrome, and Korsakoff's psychosis with mental deterioration, memory loss, and ataxia.

Prolonged alcohol use affects almost all organs of the body. Chronic drinking causes liver damage and pancreatitis. Alcohol irritates the mucosa of the digestive system, leading to gastritis, ulceration, and hemorrhage. Alcohol can also lead to malabsorption of nutrients and malnutrition (refer to Figure 20-5).

Cardiovascular effects include peripheral vasodilation (producing the flushing and sweating experienced with intoxication) and vasoconstriction of the coronary arteries. Alcohol increases the heart rate and, with chronic use, can cause cardiac myopathy, either directly or through metabolic and electrolyte imbalances. Potassium deficiency can cause cardiac arrhythmias.


Alcoholism
Complications
10%
10% of all adults are in need of alcohol treatment
Damage to brain function
Atherosclerosis
Heart failure
Liver disease
Gastric ulcer
Pancreatitis
Cancer
For women up to 3 drinks a day
For men up to 4 drinks a day
Blood tests
Heredity
Stress
Medications
Detox
Alcohol use by those under age 21
Alcohol use by pregnant women
Vitamins (B group)
Group therapy

Designua/Shutterstock.com.

Figure 20-5 Alcohol abuse is common and can cause many long-term health issues.

Alcohol Poisoning

Symptoms of acute alcoholic poisoning include cold, clammy skin; stupor; slow, noisy respirations; and alcoholic breath.

Treatment includes close observation for:

Respiratory problems. Establish and maintain airway.

Vomiting. Prevent aspirations.

Seizures. Do not require treatment unless status epilepticus occurs.

Cerebral edema. Diuretics sometimes required (e.g., mannitol).

Electrolyte imbalance. IV fluids with thiamine, folic acid, magnesium sulfate, and vitamins added ("banana bag").

Alcohol withdrawal syndromes and delirium tremens. Treated with IV BDZs.

Fetal alcohol syndrome (FAS) is a teratogenic effect of ethanol. As few as two drinks early in pregnancy has been associated with FAS, although it is more commonly noticed in infants whose mothers consumed four or five drinks per day.

Severe Alcohol Use Disorder

Symptoms of severe alcohol use disorder include:

Frequent falls and accidents
Blackouts and memory loss
Dulling of mental faculties
Irritability
Neglect of personal appearance and responsibilities

Treatment of severe alcohol use disorder can include intensive in-house rehabilitation programs in treatment facilities. Treatment frequently includes:

Vitamin B_1 (thiamine) IV, IM, or PO; multiple vitamins; and folic acid
Low-carbohydrate and high-protein diet to combat hypoglycemia
Elimination of caffeine (in coffee, tea, chocolate, and soft drinks)
Reeducation of the patient, with intensive individual, group, and family counseling, including Alcoholics Anonymous techniques

Pharmacologic Therapy

Sometimes disulfiram (Antabuse) is used, with patient cooperation, as part of *behavior modification*. Patients receive daily doses of disulfiram and are taught to expect a very unpleasant reaction such as nausea, vomiting, and sweating if even a small amount of alcohol is ingested. Although there is some evidence that drinking frequency is reduced, there is minimal evidence that it facilitates abstinence. This treatment is used less frequently because of the severe reaction potential and poor compliance.

Another treatment for alcohol use disorder includes the use of daily maintenance doses of naltrexone (ReVia), as part of counseling programs, to keep patients sober after detoxification. Naltrexone is a long-acting opiate antagonist, which acts by blocking the pleasurable sensations associated with alcohol (and opiates) and therefore lessens the desire or craving to drink. Naltrexone reduces the frequency and risk of heavy drinking but does not necessarily enhance abstinence. It is better tolerated than disulfiram because it works to decrease the desire and rewards of drinking rather than elicit a punishment for consumption.

Side effects of naltrexone are usually minor and include:

GI side effects and decreased appetite
Headache, dizziness, and anxiety
Nausea and joint pains

Caution: If naltrexone is given to someone currently dependent on opiates, it can instantly send them into severe, life-threatening withdrawal. Initiate therapy only if opiate free for 7–10 days.

Cautions or contraindications for the use of naltrexone include:
Patients with acute or severe liver problems

Patient Education

Patients taking disulfiram should be instructed regarding:

Not taking within 12 h of alcohol-containing preparations
Avoiding cough syrups, sauces, vinegars, elixirs, and other preparations containing alcohol
Caution with external applications of liniments, lotions, aftershave, or perfume
Signs of disulfiram–alcohol reaction
Reporting to emergency facility if effects do not subside or with severe reaction
Carrying identification card noting therapy
Avoiding other medications that may interact with disulfiram (e.g., metronidazole, anticoagulants, and phenytoin)

Prescription Drug Abuse

Prescription drug abuse is one of the most serious and fastest-growing problems in the United States. According to the National Institutes of Health (NIH), an estimated 52 million adult Americans have used prescription drugs for nonmedical reasons at least once in their lifetimes, about 20% of the population. About 5% of those are considered to abuse drugs chronically. Overdose is a major health issue in the United States, with around 100,000 people dying from drug overdoses in 2021. Opioids are a factor in 7 out of every 10 overdose deaths. Drug overdoses have killed over a million people since 1999.

Proper disposal and storage of prescription medications is important for deterring drug abuse. Keeping medications (especially those controlled by the Drug Enforcement Administration [DEA]) in a locked, secure space can help prevent theft, as can not letting anyone but trusted caregivers and family members know their location. Additionally, disposal of controlled medications can be done in one of four ways. (1) Disposing in the normal trash but mixing with coffee grounds or pet litter in a way that makes them undesirable for consumption. This is the preferred method, but be sure to remove any personal information from bottles upon disposal. (2) Utilizing drop-off days at local government facilities or locating a drop box (usually at a police or fire station) where you can safely dispose of medication. (3) Using a drug disposal system designed to inactivate drugs or make them unable to be accessed. Products like DisposeRX are used by putting medication in with a powder mixture and adding water to create a cement-like substance that inhibits abuse. (4) Flushing controlled medications down the toilet. Although this method is not preferred, controlled medications can be flushed if no other options are possible. Patients should be aware of their local/state Environmental Protection Agency (EPA) guidelines when considering this option and consult the FDA's "flush list" (https://www.fda.gov/drugs/disposal-unused-medicines-what-you-should-know/drug-disposal-fdas-flush-list-certain-medicines#FlushList). Although the majority of prescription drug abuse is conducted by the public, certain health care professionals have ready access to many prescription drugs, and therefore sometimes become involved in the illegal misuse of controlled substances. Prescription drugs most often abused by medical personnel are hydrocodone, oxycodone, and the BDZs. Counteractive measures include accurate recordkeeping of all controlled substances and recognition of the side effects and symptoms associated with drug abuse. Report suspected abuse to a person in authority; follow specific state agency reporting requirements.

Treatment of opiate addiction (fentanyl, oxycodone, hydrocodone, etc.) consists of a combination of counseling, behavioral therapy, and medications. Methadone, naltrexone, and buprenorphine are the medications approved for the treatment of opiate addiction. Methadone (an opioid agonist), sublingual buprenorphine (Subutex, a partial opioid antagonist), and buprenorphine with the opiate receptor antagonist naloxone (Suboxone) can be used during the detoxification process and for maintenance treatment. Naltrexone (ReVia), a pure opioid antagonist discussed earlier, is used in maintenance therapy to block the pleasurable effects of opiates.

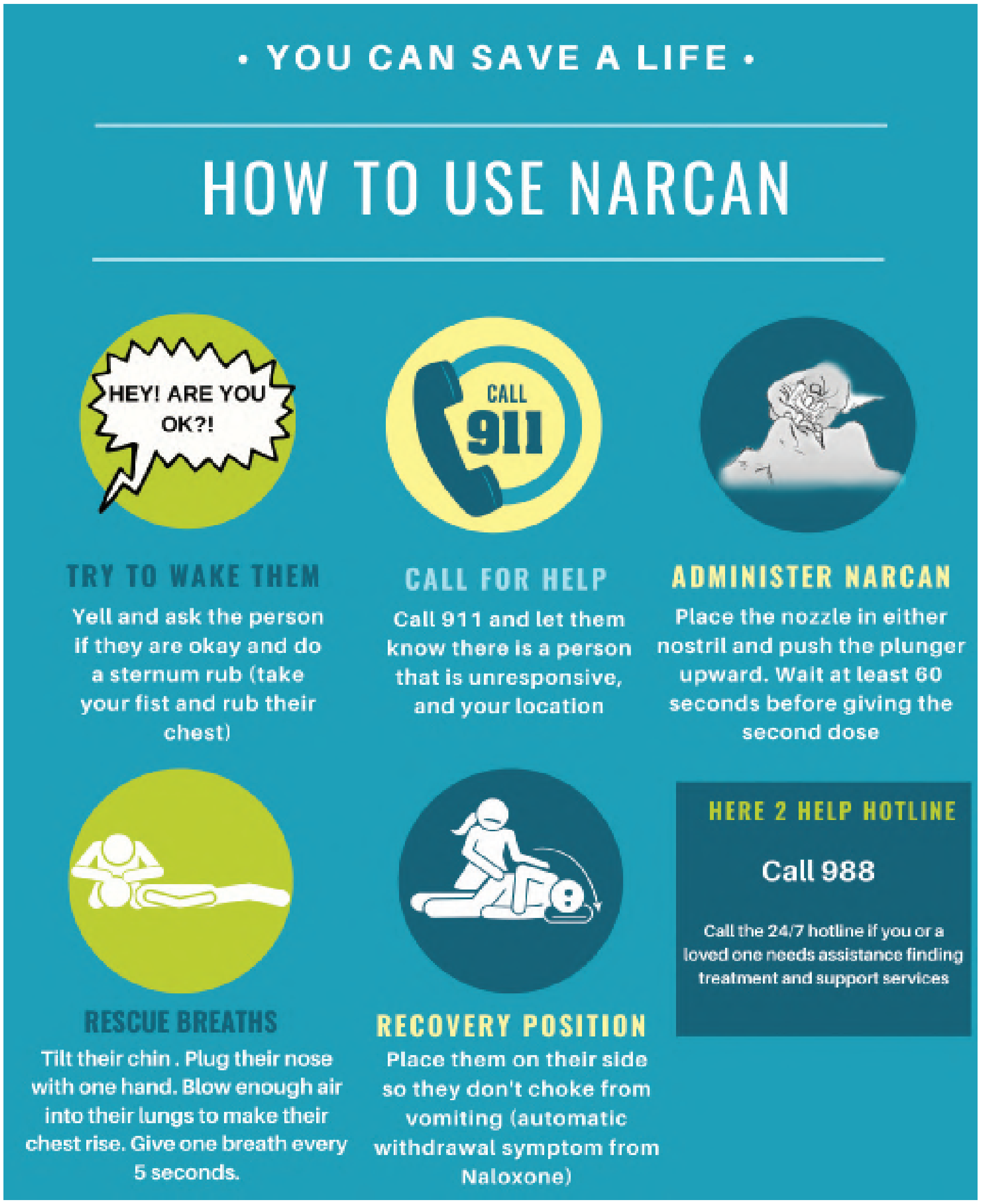
Illegal Drug Abuse

This section describes five types of substances that can be produced illegally: heroin, the amphetamines, marijuana, cocaine, and the hallucinogens (LSD and PCP).

Heroin

Heroin is an opioid drug made from morphine. Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin. People who use it do so by injecting, sniffing, snorting, or smoking. Heroin affects the body in the same way prescription opioids do. It enters the brain rapidly and binds to opioid receptors, especially those involved in feelings of pain and pleasure and those involved with controlling heart rate and breathing. Many times people who abuse heroin start with abusing prescription opioids, then switch because heroin is cheaper than prescription narcotics. In fact, a 2018 National Institute on Drug Abuse study showed that ~80% of people who abuse heroin started by abusing prescription narcotics. Heroin is extremely addictive and tolerance is achieved rapidly, meaning higher amounts are needed as time goes on.

Although there are many negative side effects from using heroin, the most dangerous effects of heroin occur as a result of overdose. When people overdose, their breathing decreases or stops completely. This decreases the amount of oxygen to the brain, causing hypoxia and sometimes death. The treatment for an overdose is the reversal agent naloxone (Narcan), which was discussed earlier in this chapter. To combat the increasing number of overdose deaths, many states have standing orders for naloxone so that pharmacies can dispense it to patients and family members without a prescription from their doctor. Figure 20-6 shows how a person would use naloxone spray in the event of a suspected opioid overdose.



• YOU CAN SAVE A LIFE •

HOW TO USE NARCAN

TRY TO WAKE THEM

Yell and ask the person if they are okay and do a sternum rub (take your fist and rub their chest)

CALL FOR HELP

Call 911 and let them know there is a person that is unresponsive, and your location

ADMINISTER NARCAN

Place the nozzle in either nostril and push the plunger upward. Wait at least 60 seconds before giving the second dose

RESCUE BREATHS

Tilt their chin . Plug their nose with one hand. Blow enough air into their lungs to make their chest rise. Give one breath every 5 seconds.

RECOVERY POSITION

Place them on their side so they don't choke from vomiting (automatic withdrawal symptom from Naloxone)

HERE 2 HELP HOTLINE

Call 988

Call the 24/7 hotline if you or a loved one needs assistance finding treatment and support services

Figure 20-6 Narcan nasal spray is administered in 3 steps.

City of Baltimore

Amphetamines

Although amphetamines can be produced and prescribed legally, they are also produced in illegal labs. Two examples are methamphetamine ("crystal," "crank," "ice," "meth," "speed") and methylenedioxymethamphetamine (MDMA, "Ecstasy").

Symptoms of chronic abuse of amphetamines include:

- ❗ Emotional lability, irritability
- Anorexia
- ❗ Mental impairment, confusion, amnesia, and neurotoxicity
- Occupational deterioration and social withdrawal
- Paranoid syndrome with hallucinations with prolonged use of high doses
- Tooth decay ("meth mouth") or ulcers of the tongue and lips

Treatment: There is no specific antidote for amphetamine overdosage. Treatment of an overdose is symptomatic and includes attention to airway, breathing, and circulation, and administration of sedative drugs such as BDZs. General physiological supportive measures include treatment for shock or cardiac irregularities as appropriate. Administration of activated charcoal may help if it can be administered within 1–2 h after the substance was ingested. External cooling devices may be used to treat hyperthermia because antipyretics are not effective in this situation.

Abrupt withdrawal of amphetamines may unmask mental health disorders. Therefore, patients require careful supervision during withdrawal, and long-term follow-up may be required because some manifestations (e.g., depression) may persist for prolonged periods.

In an attempt to temper the meth epidemic, the Combat Methamphetamine Epidemic Act of 2005 (which took effect in 2006) banned OTC sales of ingredients commonly used to make methamphetamine. Pseudoephedrine (PSE), a popular and effective oral nasal decongestant, was the primary target of the act. PSE can now be stored and sold only under special conditions ("behind the counter") by pharmacies.

Marijuana

Tetrahydrocannabinol (THC) is the active ingredient in marijuana. Although technically classified as a CNS depressant, it also possesses properties of a euphoriant, sedative, and hallucinogen. Marinol (dronabinol—a synthetic form of THC) is used as an analgesic for certain types of cancer-related pain and is approved for the prevention of chemotherapy-induced nausea and vomiting. It is also used as an appetite stimulant in cachexia associated with AIDS or cancer.

The *Cannabis* plant grows throughout the entire world, especially in tropical areas. Potency varies considerably from place to place and time to time. When not regulated, its composition varies widely, and the methods of administration do not provide a standardized and reproducible dose. To date, 38 U.S. states have legalized the use of medical marijuana for clinical use. Dispensaries with licensed pharmacists are available for patients to get prescriptions filled. Laws and regulations vary from state to state and are subject to change, so be familiar with your state's specific regulations for marijuana use. Twenty-four states have even legalized the use of recreational marijuana, while others have decriminalized its use. THC, the active ingredient released when marijuana is smoked, is fat-soluble and is stored in many fat cells, especially in the brain and reproductive organs. THC metabolizes slowly. A week after a person smokes one marijuana cigarette, 30–50% of the THC remains in the body, and four to six weeks are required to eliminate all the THC.

Side effects of marijuana include:

- Short-term memory loss, impaired learning, and slowed intellectual performance
- Perceptual inaccuracies and impaired reflex reaction (dangerous with driving)
- Apathy, lethargy, and decreased motivation

Another newer illicit drug class coming on the scene is the synthetic cannabinoids known as spice, K2, skunk, fake weed, and other names. These products, which are abused by smoking, contain dried, shredded plant material and chemical additives that are responsible for their hallucinogenic effects. Spice users report experiences similar to those produced by marijuana, but in some cases these are stronger, with unpredictable effects (rapid heart rate, hypertension, seizures, acute kidney injury, and myocardial ischemia; in a few cases spice has been associated with heart attacks). They are illegal in all states and the DEA has designated them as a Schedule I controlled substance.

Cocaine

Cocaine is a CNS stimulant and produces euphoria and increased expenditure of energy. The only approved medical use is as a local anesthetic, *applied topically only* to mucous membranes of the laryngeal, nasal, and oral cavities.

Cocaine is highly addictive, causing dependence after even short-term use. It is abused by intranasal application (sniffing or snorting), intravenous injection, and inhalation (smoking "crack"). Cocaine crosses the placental barrier and has resulted in babies who are irritable, jittery, anorexic, and seizure prone. Severe depression can be associated with withdrawal, which is a lengthy and difficult process.

Side effects of cocaine, which are serious, include:

- Hypertension, chest pain, tachycardia, cardiac arrhythmias, stroke, and cardiac/respiratory failure
- Tremor and seizures

Hallucinogens

Lysergic acid (LSD) and phencyclidine (PCP), an animal tranquilizer, are hallucinogens. They produce bizarre mental reactions and distortion of physical senses.

Side effects of hallucinogens include:

- Increased pulse and heart rate, and rise in blood pressure and temperature
- Possible physical injury to self or others due to psychotic episodes, panic, or paranoia

Dextromethorphan

Dextromethorphan (DXM), a semisynthetic morphine derivative, is a safe, effective, nonaddictive OTC cough suppressant when used appropriately. Unfortunately, DXM (primarily the one found in Robitussin and Coricidin HBP products) is often abused because of its phencyclidine-like euphoric effect at higher doses. The abuse of DXM can cause serious adverse events, such as brain damage, seizure, loss of consciousness, irregular heartbeat, and even death.

Flunitrazepam (Rohypnol)

Flunitrazepam (Rohypnol) is a potent BDZ that is not approved for use in the United States. It is used here as a recreational drug (sometimes snorted to offset cocaine withdrawal) and is known on the street as “roofies.” It has also acquired the title “date-rape drug” because of its ability to induce amnesia, preventing the victim from recalling specific events while under the influence of the drug.

The Role of Medical Personnel

The role of medical personnel in combating drug abuse includes:

- Understanding psychotropic drugs, actions, and side effects
- Willingly participating in the education of the patient, the patient’s family, and others in the community
- Giving competent care to those under the influence of drugs in a nonjudgmental way
- Recognizing drug abuse and making appropriate referrals without exception
- Complete and accurate recordkeeping of controlled stocks of drugs that could be considered potential drugs of abuse

It is the responsibility of all medical personnel not only to recognize drug abuse but also to report any observed drug abuse to the proper person in authority. Doing nothing not only enables the individual to continue to harm themself but also endangers those in their care.

There are many services available to help medical personnel deal with drug abuse. Check with your state licensing agency or certification board for information about the programs in your area, such as the Impaired Nurse program. Local mental health clinics and psychiatric facilities can also provide assistance and information. Other resources that can provide information include:

National Institute on Drug Abuse

https://nida.nih.gov

National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health

https://www.niaaa.nih.gov/

Substance Abuse & Mental Health Services Administration

https://www.samhsa.gov

Alcoholics Anonymous, Narcotics Anonymous

https://www.aa.org, https://www.na.org

DEA Recovery resources

https://www.dea.gov/recovery-resources

USA.gov (Health section includes help for substance abuse)

https://www.usa.gov/substance-abuse

Centers for Disease Control and Prevention (Alcohol Basics section includes a subsection with information on Alcohol and Other Substance Use)

https://www.cdc.gov/alcohol/fact-sheets/alcohol-and-other-substance-use.html

Case Study A

Psychotropic Drugs

A college student has been displaying “odd” behavior. The student visits the health center and reports periods of “wild activity” alternating with periods of staying in bed for days at a time. The most recent example is that they went to a high-end clothing store and maxed out their parent’s credit card, then shortly thereafter didn’t show up to any social events or classes for multiple days. The nurse reviews the patient’s records and finds that they have a history of bipolar disorder.

1. What is the drug of choice to treat patients with bipolar disorder?
   a. Buspirone
   b. Chlorpromazine
   c. Alprazolam
   d. Lithium
2. Patients on lithium should be monitored for correct dosing by which method?
   a. Observation of patient’s behavior
   b. Serum lithium levels
   c. Patient reporting of his or her own behavior
   d. EKG every three months
3. Side effects of lithium can include:
   a. Hypotension
   b. Hypertension
   c. Weight loss
   d. Hyperthyroidism
4. While reviewing the patient’s chart, the nurse notes that they had visited the health center during the prior school year with complaints of photophobia. This indicates which complication?
   a. Retinal detachment
   b. Potential seizure activity
   c. Lithium toxicity
   d. Dehydration
5. All patients should be cautioned when taking lithium with which category of medications?
   a. Anticholesterol
   b. Angiotensin-converting enzyme (ACE) inhibitors
   c. Anticoagulants
   d. Sulfonylureas

Case Study B

Psychotropic Drugs

A marine who has just completed a six-month tour of duty in Afghanistan was honorably discharged for health reasons after their unit was ambushed and many of the soldiers in their unit did not make it. They have been home for over four weeks and are experiencing signs of posttraumatic stress disorder. They are on no medication and have no allergies to medication.

1. The patient asked their physician for a medication to help them cope as they assimilate back into their daily life. What type of drug would the physician be most likely to prescribe to the patient for short-term use?
   a. Antipsychotic
   b. Anxiolytic
   c. Tranquilizer
   d. Antimanic
2. The physician warns the patient that when taking a minor anxiolytic, they may develop drug dependence. What does this likely mean?
   a. They will need larger doses over time to achieve the same effect.
   b. They will associate the drug with incidents from their tour of duty.
   c. They will find it difficult to make it through the day without the drug.
   d. They will rely on the drug during any emotional conflict.

3. The physician also explains that sudden withdrawal after prolonged use of an anxiolytic may result in which symptom?

a. Development of tics and other TDs
b. Somnolence, lethargy, and depression
c. Seizures, agitation, psychosis, insomnia, and gastric distress
d. Blurred vision and dry eyes and mouth

4. Side effects of benzodiazepines may include:

a. Akathisia
b. Neuritis
c. Dystonia
d. Ataxia

5. Physicians should use extreme caution when prescribing a benzodiazepine to a patient with a history of all the following EXCEPT:

a. Suicidal tendencies
b. History of substance abuse
c. Pregnancy and lactation
d. Type II diabetes

Chapter Review Quiz

Match the medication in the first column with the classification in the second column. Classifications may be used more than once.

Medication

1. ______ Xanax
2. ______ lithium
3. ______ Risperdal
4. ______ amitriptyline
5. ______ Prozac
6. ______ Adderall
7. ______ Buspar
8. ______ Zyprexa
9. ______ Ativan
10. ______ Wellbutrin

Classification

a. Antipsychotic
b. Anxiolytic
c. Antidepressant
d. CNS stimulant
e. Antimanic

Choose the correct answer.

11. Close monitoring of a pediatric patient taking a CNS stimulant for ADHD is necessary to assess for:

a. Temporary suppression of growth pattern
b. Alopecia
c. Weight gain
d. Hypotension

12. A side effect of a selective norepinephrine reuptake inhibitor (SNRI) for ADHD is:

a. Delayed growth
b. Insomnia
c. Increased potential for abuse
d. Increased risk of suicidal tendencies in children and adolescents

13. With depression, there may be a shortage of what substance in the brain?

a. Glucose
b. Dopamine
c. Potassium
d. Monoamine oxidase

14. A common side effect of a tricyclic is:

a. Weight loss
b. Urinary frequency
c. Mouth dryness
d. Diarrhea

15. MAOIs can interact with some drugs as well as with food and herbal supplements. These interactions can cause which side effect?

a. Hypoglycemia
b. Hypertensive crisis
c. Seizures
d. Hyponatremia

16. Tardive dyskinesia is characterized by which of the following?

a. Muscle laxity
b. Spasticity
c. Tremors
d. Involuntary, repetitive, and purposeless movements

17. What is not a treatment for alcohol use disorder?

a. Vitamin B_1 (thiamine) IV, IM, or PO; multiple vitamins; and folic acid
b. Bupropion (Wellbutrin)
c. Naltrexone (ReVia)
d. Disulfiram (Antabuse)

18. A serious side effect of cocaine is:

a. Paranoia
b. Cardiac/respiratory failure
c. Flashbacks
d. Panic attacks

19. The drug nicknamed the date-rape drug because of its ability to induce amnesia is called:

a. Rohypnol
b. Lysergic acid
c. Fluticasone
d. Phencyclidine

20. A health care provider suspects that another health care provider is abusing drugs. What is the first step that that they should take?

a. Give the individual the benefit of the doubt and remain quiet.
b. Report any observed drug use to the proper person in authority.
c. Confront the individual and threaten to tell a person in authority.
d. Provide the individual with an 800 number for drug treatment and counseling.

Chapter 21

Musculoskeletal and Anti-Inflammatory Drugs

Key Terms and Concepts

Anti-inflammatory

COX-2 inhibitors

Hormone replacement therapy (HRT)

Neuromuscular blocking agents (NMBAs)

NSAIDs

Osteoporosis therapy

Skeletal muscle relaxants

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify the commonly used skeletal muscle relaxants and their side effects.
2. List the drugs that can interact with the muscle relaxants and cause serious potentiation of effect.
3. Differentiate among the anti-inflammatory drugs and anti-rheumatic drugs.
4. Explain the serious side effects of nonsteroidal anti-inflammatory drugs (NSAIDs).
5. Explain appropriate patient education for those taking skeletal muscle relaxants and NSAIDs.
6. Describe medications for osteoporosis prevention and treatment.
7. Compare and contrast cyclooxygenase-2 (COX-2) inhibitors and other NSAIDs.

Disorders of the musculoskeletal system are rather common. Drugs used to treat such conditions may be classified into three broad categories: skeletal muscle relaxants, anti-inflammatory agents, and analgesics. This chapter will focus on NSAIDs, which, due to their anti-inflammatory and analgesic properties, are the most commonly used medication to treat musculoskeletal ailments.

Skeletal Muscle Relaxants

Some disorders of the musculoskeletal system can be attributed to structural defects (e.g., ruptured disks) that may require surgical intervention rather than medication. However, many disorders associated with pain, spasm, abnormal contraction, or impaired mobility do respond to medications classified as **skeletal muscle relaxants**. Acute, painful musculoskeletal conditions, such as backache or neck strain, are treated with a combination of muscle relaxants, rest, physical therapy, other nonpharmacological methods (e.g., hot or cold packs), and mild analgesics (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]). Muscle relaxants are given only on a short-term basis, and, after the acute pain subsides, exercises are usually prescribed by the physician or physical therapist to strengthen the weak muscles. Muscle relaxants can be used long term for certain conditions, but for acute injuries they should be used only until the problem is resolved.

Most muscle relaxant drugs affect the central nervous system (CNS; spinal cord and brain), with no direct effect on the skeletal muscle. The resulting action reduces muscle spasm; causes alterations in the perception of pain; and produces a sedative effect, promoting rest and relaxation of the affected part. Centrally acting drugs used to treat acute, painful musculoskeletal conditions include the benzodiazepines, such as diazepam (Valium) and methocarbamol (Robaxin).

A different type of muscle relaxant, dantrolene, causes a *direct* effect on skeletal muscles and is used in the management of spasticity resulting from upper motor neuron disorders such as multiple sclerosis and cerebral palsy. This medication is ineffective for amyotrophic lateral sclerosis (ALS) and is not indicated for the treatment of muscle spasms resulting from rheumatic disorders or musculoskeletal trauma (acute injuries).

Muscle relaxants also have moderate potential for abuse, as they can provide the patient with a feeling of euphoria. Benzodiazepines are classified as Food and Drug Administration (FDA) Schedule IV controlled substances. Soma (carisoprodol) is also a Schedule IV controlled substance. Although other muscle relaxants, like the commonly used baclofen and cyclobenzaprine, are not yet classified as controlled substances, health care professionals should still be aware that at high doses all muscle relaxants can exhibit the euphoric effects that can lead to abuse.

Side effects of skeletal muscle relaxants can include:

- ❗ Drowsiness, dizziness, or dry mouth
- ❗ Weakness, tremor, ataxia, and seizures
- ❗ Confusion and nervousness
- Slurred speech
- Blurred vision
- ❗ Hypotension

Cautions or contraindications for skeletal muscle relaxants apply to:

- Pregnancy or lactation
- History of drug abuse
- Impaired kidney function
- Liver disorders
- Older adults

Abrupt discontinuation

Closed-angle glaucoma

Interactions with potentiation of effect occur between skeletal muscle relaxants and:

Alcohol

Analgesics

Psychotropic medications

Antihistamines

The MedlinePlus website www.nlm.nih.gov/medlineplus/backpain.html is a good resource for patient education and written materials on back pain.

Refer to Table 21-1 for a summary of the skeletal muscle relaxants.

Table 21-1 Skeletal Muscle Relaxants

Generic Name	Trade Name	Dosage	Comments
baclofen	Lioresal	PO 10–20 mg three to four times per day; intrathecal 300–800 mcg	For spasticity associated with spinal cord injury or spinal cord diseases
carisoprodol	Soma	PO 250–350 mg three to four times per day	Caution with asthma; watch for abuse potential (C-IV controlled substance)
cyclobenzaprine	Amrix Flexeril[a]	PO 5–10 mg three times per day	Strongly anticholinergic side effects (structurally related to amitriptyline)
dantrolene	Dantrium	PO 25–100 mg two to four times per day (titrate to the lowest effective dose)	For multiple sclerosis and cerebral palsy; not for trauma or rheumatic disorders
metaxalone	Skelaxin	PO 400–800 mg q6–8h	For acute musculoskeletal conditions
methocarbamol	Robaxin	4–8 g PO daily in divided doses; also IM and IV	For acute painful musculoskeletal conditions
orphenadrine	Norflex	PO 100 mg q12h	For muscle spasm and pain
tizanidine	Zanaflex	PO 2–8 mg one to three times per day (6- to 8-h intervals)	For increased muscle tone associated with spasticity, for example, multiple sclerosis or spinal cord trauma

Note: This is a representative sample; other products are available.

[a] This brand name is no longer marketed, but the name is still commonly used.

Neuromuscular Blocking Agents

Another type of muscle relaxant that causes a direct effect on the muscles, including the diaphragm, is **neuromuscular blocking agents (NMBAs)** such as succinylcholine and rocuronium (Zemuron), used during surgical, endoscopic, or orthopedic procedures. These drugs are potentially very dangerous and can result in respiratory arrest because of the potential to paralyze the major muscle of ventilation, the diaphragm.

NMBAs are administered *only* by anesthesiologists or specially trained personnel skilled in intubation, medically induced paralysis, and resuscitation. Since these agents paralyze the muscles, analgesics and sedatives are mandatory concurrent medications because the patient can still *feel* the pain but cannot react to it.

Patient Education

Skeletal Muscle Relaxants

Patients taking skeletal muscle relaxants should be instructed regarding:

- Potential side effects (e.g., drowsiness, dizziness, weakness, tremor, blurred vision, hypotension, respiratory distress, or gastrointestinal [GI] disorders); care with driving, especially until effects are known
- Avoidance of other CNS depressants (e.g., tranquilizers, antihistamines, or alcohol) at the same time because these can cause serious CNS depression, and care with analgesics, only as prescribed by a physician
- Importance of following the physician's orders regarding rest (e.g., heat and firm mattress or bed board for back problems) and physical therapy and exercises as prescribed (after the acute pain subsides) to strengthen the weak muscles
- The acronym RICE (rest, ice, compression [elastic bandage], elevation) represents appropriate care initially for musculoskeletal injuries to extremities; a recent addition has been the focus on prevention of the injury, so some modify the acronym to PRICE
- Taking the medication only as long as absolutely necessary and observing caution regarding prolonged use, which could lead to physical or psychological dependence and withdrawal symptoms (e.g., seizures from abrupt baclofen or diazepam withdrawal after prolonged use)

Anti-Inflammatory Drugs

Anti-inflammatory drugs are used to treat disorders in which the musculoskeletal system is not functioning properly because of inflammation. Conditions such as arthritis, bursitis, spondylitis, gout, and muscle strains and sprains can cause swelling, redness, heat, pain, and limited muscle and joint mobility. Analgesics and corticosteroids are used at times for the acute stages of these disorders. The corticosteroids are not used for this purpose for extended periods of time because of potential serious side effects. However, NSAIDs, which have both analgesic and anti-inflammatory properties, are frequently given for lengthy time periods in maintenance doses as low as possible for effectiveness.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs, such as ibuprofen, inhibit the synthesis of prostaglandins, substances responsible for producing much of the inflammation and pain of rheumatic conditions, sprains, and menstrual cramps. Because of lower metabolic rates and other complications, older adults are particularly susceptible to side effects from NSAIDs and should be cautioned to report any undesirable signs or symptoms to their physician without delay.

The oldest drugs in this category are the salicylates (e.g., aspirin), which have analgesic, anti-inflammatory, and antipyretic effects. Nonsalicylate NSAIDs are tolerated better than aspirin by some patients, especially as short-term analgesics. However, with large doses and/or long-term use, they all share many of the same side effects and interactions to some degree. Patients on prolonged therapy with any of the NSAIDs should be monitored carefully. Older adults or patients in a severely weakened state do not tolerate ulceration or bleeding (which can be "silent") as well as other individuals, and most reports of fatal GI events are found in these populations.

If chronic anti-inflammatory therapy must be continued despite GI ulceration, several options for the patient are available. Ideally, after the ulcer heals, the patient could resume the NSAID with either misoprostol (Cytotec) or a proton pump inhibitor with close clinical monitoring for ulcer recurrence. Combination products are available, for example, Arthrotec, which combines diclofenac (Voltaren) with misoprostol to protect the gastric mucosa.

Diclofenac is also available topically as 1% gel and a 1.3% patch (Figure 21-1). Based on available data, topical NSAIDs seem unlikely to be associated with an increased risk of GI bleeding or renal failure. Serum concentrations of topical NSAIDs are much lower than those of oral NSAIDS; drug concentrations in meniscus, cartilage, and tendon sheath are much higher due to direct absorption of the drug through the skin into the tissues of the joints. However, until further evidence is available, the same oral NSAID warnings and precautions apply to the topical formulations as well. Topical Voltaren and generic formulations of diclofenac 1% are now available for over-the-counter use.

The FDA has issued a warning regarding the over-the-counter (OTC) nonselective NSAIDs: They should be used in strict accordance with label directions. Self-treatment with an OTC NSAID should not exceed 10 days, unless directed by a physician.

Voltaren
Emulgel
Diclofenac.
Topical anti-inflammatory agent for osteoarthritis and post-traumatic symptoms
10 g

Fahroni/Shutterstock.com.

Figure 21-1 Voltaren Gel (now generic as diclofenac) is a unique topical NSAID that can be used for specific joint problems.

COX-2 Inhibitors

Celecoxib (Celebrex) is an NSAID that exhibits anti-inflammatory, analgesic, and antipyretic activities by *selectively* inhibiting cyclooxygenase-2 (COX-2) prostaglandin synthesis. However, it does not inhibit COX-1 and therefore does not inhibit platelet aggregation (clotting) or inhibit the production of mucosal-protective prostaglandins. Consequently, it does not pose the bleeding risks of the other *nonselective* NSAIDs described previously. Due to the specific action inhibiting COX-2 prostaglandin synthesis, Celebrex (and the partially selective NSAIDs) has the *potential* to cause fewer gastric problems and poses less risk of GI bleeding unless used concurrently with aspirin.

Earlier studies have suggested that there is a "good" and a "bad" prostaglandin as far as the heart is concerned. Suppressing both types in the way nonselective NSAIDs do would theoretically help the heart. If NSAIDs are prescribed, current evidence suggests that naproxen may have the best cardiovascular safety profile. The selective **COX-2 inhibitors** shut down only the "good" prostaglandin, raising the risk of high blood pressure, atherosclerosis, and clotting. However, both traditional NSAIDs and the COX-2 inhibitors can increase the risk of adverse events (recurrent myocardial infarction [MI] or death) in patients who have a history of or who are at high risk for cardiovascular disease. Therefore, the benefits and risks in terms of pain relief and cardiovascular and GI safety must be weighed carefully for each individual.

The FDA has posted extensive NSAID (and acetaminophen) medication information at https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/nonsteroidal-anti-inflammatory-drugs-nsaids. Health care professionals are responsible for staying informed of the latest developments in this area.

Side effects of NSAIDs frequently include:

- ❗ GI ulceration and bleeding (may not be preceded by warning signs or symptoms)
- ❗ Epigastric pain, nausea, heartburn, and gastroesophageal reflux disease (GERD)
- Fluid retention and peripheral edema
- Tinnitus and hearing loss
- ❗ Rash, hypersensitivity reactions, and bronchospasm (especially with aspirin)
- ❗ Blood dyscrasias, especially prolonged bleeding time; anemia
- Liver toxicity

Cautions or contraindications for NSAIDs apply to:

- Asthma (may manifest aspirin sensitivity as bronchospasm)
- Cardiovascular disorders (e.g., hypertension, heart failure; may cause fluid retention and edema)
- Kidney disease
- Liver dysfunction
- History of GI ulcer or inflammatory bowel disease
- Blood dyscrasias, especially clotting disorders or anemia
- Children with viral infections (danger of Reye's syndrome with salicylates)

GERD

Older adults

Pregnancy and lactation

Those with aspirin and NSAID hypersensitivity

Those with sulfonamide hypersensitivity (should not take Celebrex)

These medications should be given with meals or milk to reduce GI side effects. Enteric-coated, timed-release capsules or buffered aspirin are sometimes also recommended to reduce gastric irritation.

Interactions of NSAIDs (especially salicylates) are many, but the most important clinically occur with:

Alcohol (potentiates the possibility of GI bleeding)

Anticoagulants (potentiate the possibility of bleeding; also true of vitamin E)

Corticosteroids (increase the chance of GI effects with prolonged administration of NSAIDs)

Aspirin (increases adverse GI effects and diminishes the risk-reducing effects of COX-2 inhibitors in the GI tract); nonselective NSAIDs may decrease the antiplatelet effects of aspirin (give the NSAID 30 min after or 8 h prior to aspirin ingestion)

Antihypertensives (attenuated response)

Lithium (decreased clearance)

Methotrexate (potentiates and increases the risk of methotrexate toxicity)

Uricosurics (probenecid or sulfinpyrazone), whose action is antagonized by salicylates

Refer to Table 21-2 for a summary of the NSAIDs.

Table 21-2 Nonsteroidal Anti-Inflammatory Drugs

Generic Name	Trade Name	Dosage
Nonselective (Traditional) NSAIDs		
diclofenac	Voltaren DR[a]	PO 150–225 mg daily in divided doses
	Voltaren XR	PO 100 mg one to two times per day
	Voltaren	Gel 2–4 g four times per day depending on the site (use supplied dosing cards)
	Flector	1 patch bid
ibuprofen	Motrin	PO 200–800 mg four times per day
	Motrin IB, Advil (OTC)	PO 200–400 mg q4–6h (max 1,200 mg per day, 10 days max)
	Caldolor	IV 400–800 mg q6h over 30 min (for hospitalized patients unable to take PO for pain or fever)

(Continued)

Table 21-2 Nonsteroidal Anti-Inflammatory Drugs (*continued*)

Generic Name	Trade Name	Available As
indomethacin	Indocin	PO, R up to 200 mg daily in divided doses
ketorolac	(Toradol)[a]	PO 20 mg one time, and then 10 mg q4–6h (5 days max); IM/IV 15–30 mg q6h (5 days max)
naproxen	Naprosyn, Anaprox	PO 250–550 mg bid (q12h)
	Aleve (OTC)	PO 220 mg q8–12h (max 660 mg per day, 10 days max)
oxaprozin	Daypro	PO 600–1,200 mg once daily
piroxicam	Feldene	PO 10–20 mg dailyto bid
sulindac	Sulin	PO 150–200 mg q12h
Partially Selective NSAIDs		
etodolac	Lodine[a]	PO 600–1,200 mg daily in divided doses
meloxicam	Mobic	PO 7.5–15 mg daily or bid
nabumetone	Relafen[a]	PO 1,000–2,000 mg daily
Selective COX-2 Inhibitor		
celecoxib	Celebrex	PO 100–200 mg daily or bid
Combinations		
diclofenac/misoprostol	Arthrotec 50, 75	PO 50 mg three to four times per day; 75 mg bid

[a] This brand name is no longer marketed, but the name is still commonly used.

Note: Other NSAIDs are available. This is a representative list.

Clinical Connection

Medication Reconciliation

In an ideal world, each patient would only go to one doctor who treats all their conditions and prescribes all their medications, which are all filled at the same pharmacy. This would drastically cut down on gaps in care, duplications in therapy, and potentially dangerous drug interactions. As we know, this is not the case; therefore, it is important to always take the time to get a complete list of medications that the patient is taking, including OTC medications. This practice is known as medication reconciliation and is a useful tool to identify potential problems in a medication regimen. Analgesics such as acetaminophen and NSAIDs are available both as prescriptions and OTC, so they are commonly involved in therapeutic duplications and interactions. NSAIDs are especially problematic because there is such a wide range of drugs, and the names of these drugs are not similar. For example, a patient may be on Celebrex (celecoxib) for arthritis and be taking ibuprofen OTC for headaches. This patient is at an increased risk for stomach ulcers, kidney problems, and other side effects. Although there are many examples that could be given, proper medication reconciliation will help to avoid these types of situations, especially with medications like NSAIDs that are readily available and commonly prescribed, yet still have potential for serious adverse effects.

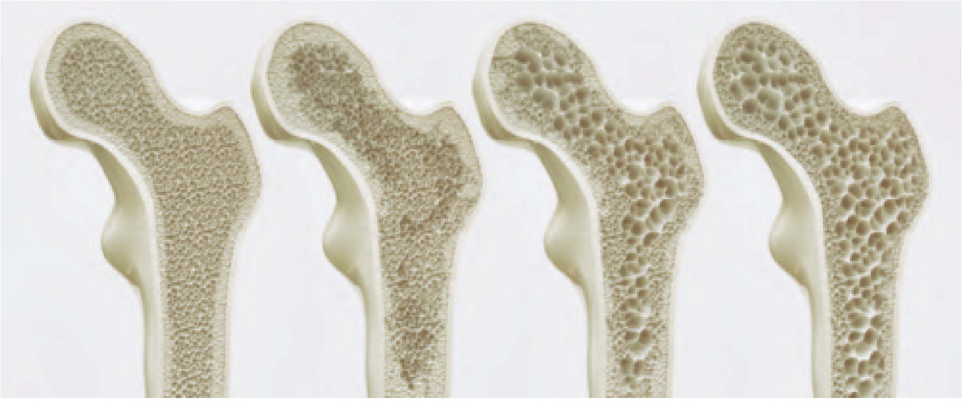
Patient Education

Patients taking NSAIDs should be instructed regarding:

- Administering the medication with food to reduce gastric irritation
- Caution with dosage (to reduce the chance of overdose, follow the physician's directions carefully regarding the amount of drug)
- Discontinuing the drug and reporting to the physician any sign of abnormal bleeding (gums, stool, urine, and bruising), epigastric pain or nausea, ringing in the ears or hearing loss, visual disturbances, weight gain or edema, and skin rash
- Avoiding taking any other drugs, either prescribed or OTC, without checking first with a physician or pharmacist regarding possible interactions and duplication of the medication
- Avoiding taking large amounts of aspirin or other NSAIDs with kidney, liver, or heart disease or with a history of GI ulcer (with these conditions, take only under medical supervision); patients with asthma may manifest sensitivity to aspirin and other NSAIDs
- The danger that GI ulceration and bleeding can occur without previous warning signs or symptoms
- Discontinuing NSAIDs before elective surgery or dental procedures to reduce the risk of serious bleeding (check with the physician or dentist)
- Not taking Celebrex if allergic to sulfa

Osteoporosis Therapy

Osteoporosis (porous bone) is defined as a systemic skeletal disease characterized by low bone mass and deterioration of bone tissue, leading to bone fragility and increased susceptibility to fracture, especially of the hip, spine, and wrist (Figure 21-2). It most commonly affects older populations, primarily postmenopausal females. The diagnosis of osteoporosis is determined by measuring one's bone mineral density (BMD), which serves as a predictor of future fracture risk. **Osteoporosis therapy** includes calcium and vitamin D supplementation and several prescription medications currently approved for the prevention and/or treatment of osteoporosis. Calcium and vitamin D supplementation should be started at the first sign of osteoporosis and in all patients who are considered to be at risk because of age, sex, or family history.



Crevis/Shutterstock.com

Figure 21-2 Bones affected by osteoporosis become progressively porous as the disease progresses and becomes more severe. The less dense a bone is, the more easily it can break when stress (like a fall) is applied.

Bisphosphonates

Bisphosphonates are nonhormonal agents that act directly to inhibit bone reabsorption, thereby increasing bone mineral density at the spine and hip, as well as decreasing the incidence of first and future fractures. Alendronate (Fosamax), ibandronate (Boniva), and risedronate (Actonel) have been approved for both the prevention and treatment of osteoporosis and are considered the first-line therapy. The bisphosphonates are also indicated for management of Paget's disease of the bone, a chronic disorder characterized by fractures, skeletal abnormalities, and significant bone pain.

Bisphosphonates bind strongly to and accumulate in bone, creating a reservoir of drug that is released back into systemic circulation gradually over a period of months or years after the treatment is stopped. Beneficial effects on BMD persist for some time, suggesting that a "drug holiday" could mitigate some of the risks associated with bisphosphonate therapy.

A bisphosphonate, Reclast (zoledronic acid), is a once-yearly infusion that has been shown to significantly decrease the risk of fractures and also to increase bone mass. It is the most potent bisphosphonate, but patients who are on it should be checked for proper renal function before starting it and should be monitored throughout therapy. Other side effects and warnings are similar to those of other bisphosphonates.

Side effects of bisphosphonates can include:

- ❗ GI distress (nausea, dyspepsia, and esophagitis)
- Abdominal and chest pain; bone and musculoskeletal pain

Caution with bisphosphonates applies to active upper GI problems, for example, dysphagia, GERD, gastritis, and ulcers.

Cautions or contraindications for bisphosphonates apply to:

- Hypocalcemia
- Renal failure
- Drugs associated with gastric irritation (ASA, NSAIDs)
- Inability to sit upright for 30–60 min after taking the drug

Patient Education

Patients taking bisphosphonates should be instructed regarding:

- The importance of taking the medicine with a full glass of water (6–8 oz) at least 30 min before the first food, beverage, or medication of the day
- Not lying down or eating or drinking anything else for at least 30–60 min to prevent reflux and avoid esophageal irritation
- Contacting the health care provider if there is pain while swallowing, difficulty swallowing, worsening heartburn, or thigh or groin pain
- Taking supplemental calcium and vitamin D if dietary intake is inadequate
- Performing weight-bearing exercises
- Modifying cigarette smoking and alcohol and caffeine consumption, if these factors exist

Hormones

Estrogens

Before menopause, estrogen helps to maintain a normal bone reabsorption rate in females. **Hormone replacement therapy (HRT)**—estrogen with or without progestin—is recommended for postmenopausal osteoporosis prevention (secondary to estrogen deficiency) *only* when patients are unable to take other agents and when the benefits outweigh risks. The FDA recommends prescribing the lowest possible dose for the shortest period of time. If HRT is started soon after menopause, estrogen prevents the accelerated phase of bone loss that occurs in the first five years after the onset of menopause.

Selective Estrogen Receptor Modifiers

Raloxifene (Evista) is a selective estrogen receptor modifier (SERM) with estrogen agonist activity on bone and lipids, and estrogen antagonist activity on breast and uterine tissue. These properties result in increased bone mineral density, decreased bone reabsorption, and reduced fracture risk without promoting breast or endometrial cancer.

The incidence of vaginal bleeding and breast tenderness is lower with raloxifene than with HRT. However, in contrast to HRT, raloxifene can cause hot flashes and muscle cramps in the legs. Raloxifene is contraindicated in pregnancy and females with a history of thromboembolic disorders.

Calcitonin

A synthetic form of the hormone calcitonin is available as a nasal spray (Miacalcin) or as a subcutaneous injection for the treatment of postmenopausal osteoporosis in females who are more than five years past menopause. Calcitonin is involved with calcium regulation, increases spinal bone density, and provides an analgesic effect in acute vertebral fractures. Calcitonin is reserved for females who refuse or cannot tolerate HRT or in whom HRT is contraindicated. Local nasal effects (e.g., irritation, redness, rhinitis, and epistaxis [nosebleed]) are the most common adverse effects from the nasal spray.

Store the unopened bottle of calcitonin in the refrigerator. Once the pump has been activated, store at room temperature in an upright position. Discard all unrefrigerated bottles after 30 days.

Parathyroid Hormone

Teriparatide (Forteo) is an injectable form of parathyroid hormone approved for postmenopausal females and males with osteoporosis who are at a high risk for having a fracture. It increases GI calcium absorption and renal tubular reabsorption of calcium, increasing bone mineral density, bone mass, and strength. Common adverse effects include nausea, hypotension, dizziness, arthralgia (joint pain), and leg cramps. Safety and efficacy beyond two years has not been established and is not recommended.

Monoclonal Antibodies

Prolia (denosumab) is a treatment option for osteoporosis in both males and females. It works by inhibiting osteoclast (responsible for bone resorption) activity and is normally reserved for patients who are at a high risk of fracture or have proven to be intolerant to traditional therapy. Prolia is a subcutaneous injection and is given biannually. It is commonly used in combination with calcium and vitamin D supplementation and Forteo (teriparatide).

Post Menopausal Osteoporosis Treatments

Some newer drugs have been approved that are specifically designed for menopausal and postmenopausal females. A mixture of conjugated estrogens and bazedoxifene (Duavee) is specifically indicated for the prevention of postmenopausal osteoporosis. This drug is taken during menopause and helps to lower the risk of developing osteoporosis later. Romosozumab (Evenity) is a monoclonal antibody that works in two ways. It increases the activity of bone-building cells and it slows down bone loss by decreasing bone-removing activity. This treatment is reserved for females with a history of osteoporotic fracture or multiple risk factors for fracture, or those who have failed or are intolerant to other osteoporosis therapies.

Refer to Table 21-3 for a summary of osteoporosis therapy.

Table 21-3 Agents for Osteoporosis Prevention and Therapy

Generic Name	Trade Name	Prevention Dose	Treatment Dose	Comments
Hormones				
Selective Estrogen Receptor Modifier				
raloxifene	Evista	PO 60 mg daily	PO 60 mg daily	Can be given without regard to meals
Bazedoxifene and conjugated estrogens	Duavee	PO 20 mg / 0.45 mg daily	PO 20 mg / 0.45 mg daily	Also indicated for vasomotor symptoms associated with menopause
Calcitonin–Salmon				
calcitonin–salmon	Miacalcin	Not indicated	Intranasally 200 units (one activation) daily	Alternate nares
Parathyroid Hormone				
teriparatide	Forteo	Not indicated	SQ 20 mcg daily	For up to 2 years
Bisphosphonates				
alendronate	Fosamax	PO 5 mg daily ac	PO 10 mg daily ac	Refer to patient education
		PO 35 mg qwk ac	PO 70 mg qwk ac	
			PO 40 mg daily ac for 6 months	For Paget's disease
ibandronate	Boniva	PO 2.5 mg daily ac	PO 2.5 mg daily ac	Refer to Patient Education
		PO 150 mg qmo	PO 150 mg qmo	
			IV 3 mg bolus q3 months (over 15–30 sec)	
risedronate	Actonel	PO 5 mg daily ac	PO 5 mg daily ac	Refer to Patient Education
		PO 35 mg qwk ac	PO 35 mg qwk ac	
		PO 150 mg qmo	PO 150 mg qmo	

Generic Name	Trade Name	Prevention Dose	Treatment Dose	Comments
zoledronic acid	Reclast	IV 5 mg every 2 years	PO 30 mg daily ac for 2 months IV 5 mg every 1 year	For Paget's disease Should be infused over at least 15 min
Monoclonal antibodies				
denosumab	Prolia	—	SC 60 mg every 6 months	Supplement with calcium and vitamin D Also used for certain cancers
romosozumab	Evenity	—	SC 210 mg every month for 12 months	Indicated for postmenopausal females with a high risk of fracture

Note: Other dosing regimens are available.

Case Study A

Musculoskeletal Drugs

A patient pulled a muscle in their back while helping their child move into college. The patient is now experiencing severe back spasms.

1. The patient visits their primary care physician, who prescribes cyclobenzaprine, a skeletal muscle relaxant. The physician cautions the patient that they might experience which side effect?

a. Hypertension
b. Euphoria
c. Palpitations
d. Insomnias

2. The patient's physician also explains that this medication should be taken for which time frame?

a. Intermittently as needed
b. Short term
c. Minimum of 6 months
d. 1 year

3. The physician reviews the patient's past medical history to determine if they have a condition that would require caution. What is an example of this type of condition?

a. Past history of muscle strain
b. Cataracts
c. Impaired kidney function
d. Past history of appendicitis

4. After prescribing the medication, the physician cautions the patient to be careful in taking other medications with this muscle relaxant. What is one category of medication that may cause a potentiated effect?

a. Antiemetics
b. Anticoagulants
c. Anticholinergics
d. Antihistamines

5. The patient has been taking cyclobenzeprine for two days. They have experienced some relief from the back spasms, but now is complaining of a dry mouth. What action would the physician take after hearing about this symptom?

a. Advise the patient to discontinue the medication immediately.
b. Advise the patient to take an antihistamine, as they might be experiencing an allergic reaction.
c. Explain that this is a common side effect.
d. Inquire if the patient is experiencing urinary urgency.

Case Study B

Anti-Inflammatory Drugs

A patient has been experiencing pain in their right knee. After examination of the knee, the nurse practitioner (NP) recommends taking an NSAID.

1. The NP explains that the medication's action is to reduce inflammation by:
   a. Increasing the synthesis of prostaglandins
   b. Inhibiting the synthesis of prostaglandins
   c. Reducing white blood cells in the affected joint
   d. Increasing blood flow to the affected joint

2. Which age group is particularly susceptible to side effects from NSAIDs?
   a. Young children
   b. Young adults
   c. Postmenopausal females
   d. Older adults

3. A frequent side effect of NSAIDs is:
   a. Diarrhea
   b. Urinary frequency
   c. Hypotension
   d. GI ulceration and bleeding

4. To reduce the potential side effects while taking NSAIDs, the NP suggests that the patient:
   a. Take the medication with a small sip of water
   b. Take the medication with meals
   c. Avoid enteric-coated capsules
   d. Take the medication on an empty stomach

5. The patient expresses concern about taking medication, including the NSAID. What would be the most appropriate explanation from the NP regarding NSAIDs and the risk of cardiovascular disease?
   a. NSAIDs are not safe for patients with a history of cardiovascular disease.
   b. NSAIDs have a greater GI risk than cardiovascular risk.
   c. NSAIDs have no risk.
   d. NSAIDs can increase the risk of adverse events for individuals with a history of cardiovascular disease.

Chapter Review Quiz

Match the medication in the first column with the appropriate classification in the second column. Classifications may be used more than once.

Medication

1. ___ Dantrolene
2. ___ Arthrotec
3. ___ Mobic
4. ___ Actonel
5. ___ Voltaren
6. ___ Flexeril
7. ___ Nabumetone
8. ___ Evista
9. ___ Celebrex

Classification

a. Combination NSAID
b. Osteoporosis therapy
c. Muscle relaxant for multiple sclerosis
d. Muscle relaxant for acute muscle strain
e. Partially selective NSAID
f. Nonselective NSAID
g. COX-2 inhibitor

Choose the correct answer.

10. Patients with which respiratory condition may manifest a sensitivity to aspirin and other NSAIDs?

a. Allergies
b. Frequent upper respiratory infections
c. Cystic fibrosis
d. Asthma

11. A patient who is taking an NSAID develops ringing in the ears. What action should they be instructed to take?

a. Discontinue the drug.
b. Go immediately to the emergency department.
c. Make an appointment with an audiologist.
d. Reduce the dosage by half.

12. The mechanism of action of bisphosphonates is to:

a. Increase bone development
b. Increase bone resorption
c. Inhibit bone resorption
d. Increase calcium deposition into the bone

13. Which of the following is a selective estrogen receptor modifier?

a. Alendronate
b. Raloxifene
c. Teriparatide
d. Calcitonin-salmon

14. What is a key point to review with a patient taking a bisphosphonate?

a. Taking NSAIDs for discomfort

b. Avoiding weight-bearing exercise

c. Increasing caffeine consumption

d. Sitting upright for 30–60 min after taking the drug

15. Combining salicylates and alcohol increases the risk for:

a. Anemia

b. The possibility of GI bleed

c. Reye's syndrome

d. The possibility of accelerated clotting time

16. Unless otherwise directed by a physician, what is the maximum number of days that an OTC NSAID should be taken?

a. 3

b. 7

c. 10

d. 14

17. The muscle relaxant dantrolene is used to treat:

a. Amyotrophic lateral sclerosis (ALS)

b. Rheumatic disorders

c. Poststroke contractures

d. Spasticity associated with cerebral palsy

18. Suppose NSAIDs are suggested as a treatment for a lengthy time period. How will they most likely be prescribed?

a. Variable doses on consecutive days

b. Alternate day dosing

c. A dose as low as possible for effectiveness

d. A 3-day drug holiday once a month

19. Which drug category may potentiate the possibility of bleeding when taking NSAIDs?

a. Multivitamins

b. Antianxiety drugs

c. Antihistamines

d. Anticoagulants

20. Which medication for osteoporosis would be a poor choice in a patient who has stage III renal failure?

a. Calcium and vitamin D supplementation

b. Actonel

c. Prolia

d. Reclast

Chapter 22

Anticonvulsants, Antiparkinsonian Drugs, and Agents for Alzheimer's Disease

Key Terms and Concepts

Absence seizures
Alzheimer's disease (AD)
Anticholinergics
Anticonvulsants
Antiepileptic drug (AED) therapy
Antiparkinsonian drugs
Drug-induced parkinsonism (DIP)
Epilepsy
Febrile seizures
Focal (partial) seizures
Mixed seizure
Neuroleptic malignant syndrome
Parkinson's disease (PD)
Primary generalized seizures
Psychomotor epilepsy
Restless legs syndrome (RLS)
Status epilepticus
Temporal lobe seizures
Tonic-clonic seizures
Unilateral seizures

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe the different types of seizures.
2. List the medications used for each type of epilepsy and common side effects.
3. Describe the drug therapy for febrile seizures.
4. List the drugs used for parkinsonism and common side effects.
5. Describe the patient education appropriate for those receiving anticonvulsants and antiparkinsonian drugs.
6. Describe the drug therapy for the treatment of restless legs syndrome.
7. Describe the drugs for the treatment of Alzheimer's disease.

Anticonvulsants

Seizures are brief, abnormal neuronal discharges in the brain that occur repeatedly for a variable length of time. Seizures can appear to be random, with no clear cause, or can be the result of another condition or acute injury (such as a traumatic brain injury from a car crash). **Anticonvulsants** are used to reduce the number or severity of seizures in patients with epilepsy. **Epilepsy**, which is defined as two or more unprovoked seizures separated by 24 h, is characterized by sudden attacks of altered consciousness, motor activity, or sensory impairment. Epilepsy affects over 5 million people in the United States, and is one of the most common neurological disorders along with migraine, stroke, and Alzheimer's disease.

Treatment is based on the type, severity, and cause of seizures. Although less than half of epileptic seizures have an identifiable cause, seizures may sometimes be associated with cerebrovascular disease, cerebral trauma, intracranial infection or fever, brain tumor, intoxication, or chemical imbalance. Sometimes the underlying disorder can be corrected—for example, fever, hypoglycemia, or electrolyte imbalance—and anticonvulsive medicine is not indicated.

Some medications can lower a person's seizure threshold and should be used with extreme caution in patients who have a history of seizures or are at acutely high risk for seizures (such as those with a recent head injury). There are many drugs that affect the seizure threshold, but the most common ones are bupropion, amitriptyline, clozapine, amphetamines, cyclobenzaprine, diphenhydramine (Benadryl), methotrexate, and tramadol and other opioids. Initiating these drugs or adjusting their doses should be done by a neurologist for patients who have a history of seizures.

Seizures are described in two major groups that are differentiated by how and where they begin in the brain:

1. ***Primary generalized seizures***—begin with widespread electrical discharge that involves both sides of the brain at once. The result is bilaterally symmetrical and without local onset; further classified as convulsive (tonic, clonic, and tonic-clonic) or nonconvulsive (absence, myoclonic, and atonic).
2. ***Focal seizures*** (also known as partial seizures)—begin with an electrical discharge in one limited area of the brain. If there is no loss of consciousness, it is classified as a simple focal (partial) seizure. If there is loss of consciousness, it is called a complex focal (partial) seizure. Less than 15% of all seizures are of this type.

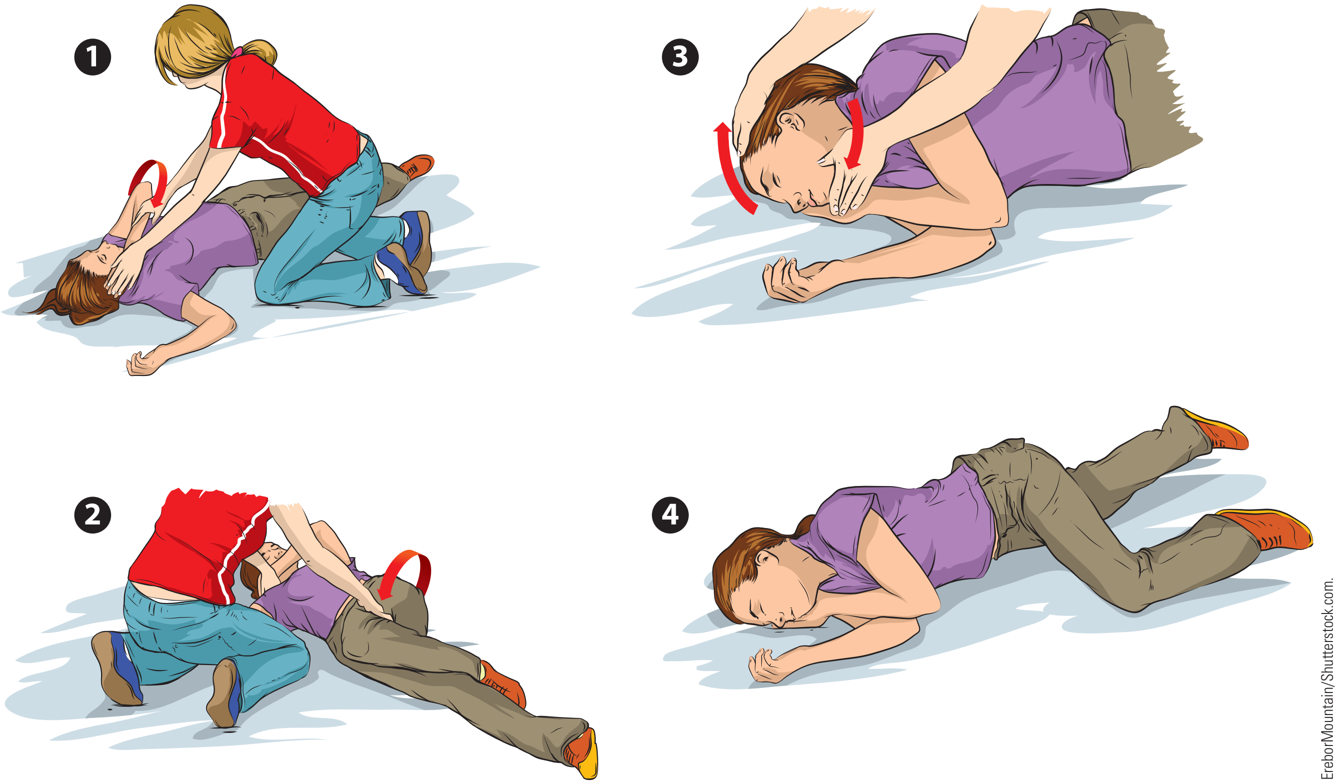
Treatment failure can be the result of inappropriate selection of an anticonvulsant for the specific type of seizure. For example, carbamazepine is used to treat many types of seizures; however, it is well known that it aggravates myoclonic and absence seizures. Drug therapy is individualized, and the selection of the most appropriate drug is based on the seizure type and other patient factors. Once the treatment is started, approximately 50% of patients achieve adequate seizure control with monotherapy (one drug).

Primary Generalized Seizures

Generalized seizures include *tonic-clonic* (formerly called *grand mal*) and *absence* (formerly called *petit mal*) seizures and occur in about 40% of patients with epilepsy. *Tonic* pertains to tension or contraction, particularly muscle contraction. **Tonic-clonic**

seizures are characterized by an abrupt loss of consciousness and falling, with tonic extension of trunk and extremities (tonic phase), followed by alternating contraction and relaxation of the muscles (clonic phase). The attack usually lasts 2–5 min, and urinary and fecal incontinence may occur. During the recovery period, patients are confused and sleepy and may complain of a headache.

Initial treatment consists *only* of preventing injury by removing any objects that could cause trauma; cushioning the head and turning it to the side; and loosening tight clothing, especially collars and belts. Do not try to open the mouth or force anything between the teeth. Refer to Figure 22-1.



EreborMountain/Shutterstock.com.

Figure 22-1 Bystanders should never attempt to inhibit the movement of a person who is having a seizure. The only action should be to safely assist them to the ground if needed, ensure the area is safe, and move them onto their side.

Clinical Connection

Driving with Seizure-Related Conditions

Given the symptoms of seizures, it is understandable that, to protect both themselves and others from potential harm, it is not advisable for a person who has uncontrolled seizures to operate a vehicle. Even though this may seem logical, there are currently no definitive laws prohibiting those affected with seizures from driving if they already have a valid driver's license. Instead, patients rely on the advice of their physician or other health care provider. In general, it is recommended that a person who has been diagnosed with an acute seizure disorder (from a car accident or other head trauma) should be symptom free for three to six months before resuming driving. For a person with a chronic seizure condition, it is recommended that the seizures be controlled for one to two years before driving. Although these are recommendations and not laws, patients should be informed that they will be held liable for accidents that may occur if they drive against physician recommendations. Additionally, it should be noted that laws and regulations vary by state.

If seizures are prolonged or so frequent that the patient does not regain consciousness between seizures, the condition is known as **status epilepticus** and is considered to be a true neurologic emergency. This condition has a reported fatality rate of up to 30%–40% after diagnosis. The treatment of choice is IV lorazepam (Ativan) administered slowly. Simultaneous loading with IV phenytoin or fosphenytoin is also recommended. In addition, if the cause of status epilepticus is known, reversal of the cause should be immediately addressed.

Absence seizures, previously called petit mal, are so called because of the absence of convulsions. They are characterized by a sudden onset and a brief 10–20-sec loss of consciousness with no falling, and usually occur initially in children. This can appear as staring into space. Absence seizures are not associated with postrecovery drowsiness. Patients with childhood absence epilepsy frequently achieve remission with increasing age or treatment.

Febrile seizures are the most common childhood seizure disorder, occurring in approximately 3% of children ages 6 months to 6 years. Their presence may signify a serious underlying acute infection such as sepsis or bacterial meningitis. Most febrile seizures are “simple”—single, brief (less than 15 min in duration), and generalized. Resolving the underlying condition is generally sufficient treatment for these types of seizures, and daily medication is not necessary.

Focal (Partial) Seizures

Focal (partial) seizures (also known as **psychomotor epilepsy** or **temporal lobe seizures**) account for up to 60% of new cases of epilepsy. They are caused by a lesion in the temporal lobe of the brain and are limited to one cerebral hemisphere. Most seizures last from 10 sec to 5 min. Complex symptoms can include confusion, impaired understanding and judgment, staggering, purposeless movements, bizarre behavior, and unintelligible sounds, but no convulsions. A focal (partial) seizure may be preceded by a subjective but recognizable sensation (an aura) that a seizure is going to occur.

Unilateral seizures affect only one side of the body. Some patients may have **mixed seizure** patterns combining more than one type. It is important to observe and report the type and length of seizures and general responsiveness to medications.

Drug Therapy for Generalized and Partial Seizures

First-Generation Anticonvulsants

Prophylactic treatment of *generalized and partial seizures when indicated* should be started with a single drug such as valproate, lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, or phenytoin. The dosage should be started at the lowest dose possible and be titrated to the point that seizure control is achieved or until the maximally tolerated dose is reached. The aim of this therapy is to prevent seizures without oversedation, and the dosage is adjusted according to the individual patient response and serum drug levels when available.

Side effects of phenytoin can include:

- ❗ Sedation, ataxia, dizziness, and headache
- ❗ Blurred vision, nystagmus, and diplopia
- ❗ Rash and dermatitis, Stevens–Johnson syndrome (a severe inflammatory disease affecting children and young adults), and lupus-like symptoms (chance of these side effects is reduced with proper titration)

Megaloblastic anemia (treated with folic acid)

Osteomalacia (bone softening, treated with vitamin D)

Cautions or contraindications with phenytoin apply to:

Kidney or liver disease

Diabetes

Heart failure, bradycardia, heart block, and hypotension

Pregnancy and lactation

Hematological disease

Abrupt discontinuation

There are many drug ***interactions*** and food or nutrient interactions with phenytoin, including:

Cimetidine, isoniazid, salicylates, selective serotonin reuptake inhibitors (SSRIs), sulfonamides, topiramate, and trimethoprim may increase the levels of phenytoin.

Phenytoin may decrease the effectiveness of "azole" antifungals, carbamazepine, estrogens, oral contraceptives, protease inhibitors, certain antidepressants and antipsychotics, valproic acid, and "statins."

Another medicine sometimes used for partial, generalized, or mixed seizures is carbamazepine (Tegretol). It has the advantage of minimal sedation and cognitive adverse effects.

Side effects of carbamazepine can include:

Ataxia, syncope (fainting), and visual difficulties

Risk for hyponatremia (decreased level of sodium in the blood)

❗ Cardiac, hematological, kidney, liver, and pancreas complications

Rash, for example, Stevens–Johnson syndrome more likely to occur in Asian patients who test positive for an inherited variant of an immune system gene; FDA recommends genetic testing of patients of Asian descent prior to starting therapy

Multiple ***interactions*** of carbamazepine occur with:

Phenytoin, phenobarbital, and rifampin (decrease levels of carbamazepine)

Calcium channel blockers, cimetidine, macrolides (e.g., erythromycin), azole antifungals, certain antipsychotics, protease inhibitors, valproic acid, and isoniazid (increase levels of carbamazepine)

Warfarin (increased metabolism, decreased effect)

Grapefruit juice potentiates action and can increase the risk of serious adverse effects; do not take grapefruit juice with carbamazepine

Oxcarbazepine (Trileptal), a second-generation oral anticonvulsant indicated for the treatment of partial seizures, is an analogue of carbamazepine. It is as effective as the first-generation agents and may be less likely than carbamazepine to cause CNS side effects and hematological abnormalities. Oxcarbazepine does not generally require drug level monitoring, and it appears to have less significant drug interactions.

Note

The FDA has alerted health care professionals of an increased risk of suicidal ideation and behavior in patients receiving anticonvulsants to treat epilepsy, psychiatric disorders, or other conditions (e.g., migraine, neuropathic pain). All patients beginning treatment with anticonvulsants or currently receiving such treatment should be closely monitored for emerging or worsening suicidal thoughts and behavior, depression, and/or unusual changes in mood or behavior.

Valproic acid (Depakene, Depakote) is considered a broad-spectrum anticonvulsant useful for the management of many seizure types, including generalized tonic-clonic, absence, and myoclonic seizures. Dosage adjustments may be needed in hepatic diseases.

Side effects of valproic acid include:

❗ Weight gain and dyspepsia

❗ Alopecia, rash, and tremor

❗ Hepatotoxicity, life-threatening pancreatitis (black box warning), and blood dyscrasias

Multiple ***interactions*** of valproic acid occur with:

Carbamazepine, phenytoin, phenobarbital protease inhibitors, and rifampin (decrease valproic acid levels)

Chlorpromazine, felbamate, guanfacine, salicylates, and topiramate (increase valproic acid levels or effects)

Drug Therapy for Febrile Seizures

Routine treatment of febrile seizures involves searching for the cause of the fever and taking measures to control the fever (e.g., with the use of antipyretics). Most children with febrile seizures do not require anticonvulsant drugs. Those that do may be treated with diazepam rectal gel if the seizure lasts longer than 5 min. The American Academy of Pediatrics Subcommittee on Febrile Seizures does not currently recommend continuous or intermittent **antiepileptic drug (AED) therapy** for children with one or more simple febrile seizures. A decision to use prophylactic AEDs for children with complex febrile seizures should be made on an individual basis, taking into account the underlying risk factors for recurrence.

Drug Therapy for Absence Seizures

The drug of choice for the management of absence epilepsy is often ethosuximide (Zarontin), which is effective only for this type of epilepsy and lacks the idiosyncratic hepatotoxicity of valproic acid. Other drugs sometimes used in the treatment of absence seizures, when Zarontin is ineffective, include clonazepam (Klonopin), valproic acid (Depakene), and lamotrigine (Lamictal).

Side effects of the drugs used for absence epilepsy can include:

❗ Sedation, dizziness, headaches, aggression, or irritability

❗ Gastrointestinal (GI) distress, including anorexia, nausea, vomiting, and diarrhea (take with food to minimize these effects)

Rash and blood dyscrasias

Cautions or contraindications with drugs used for absence epilepsy apply to:

Hepatic or renal disease

Pregnancy and lactation

Pancreatitis (with valproate)

Abrupt discontinuation

Interactions occur between ethosuximide and:

Carbamazepine, phenytoin, primidone, phenobarbital, valproic acid, rifampin, isoniazid, and antiretroviral protease inhibitors

Alternative formulations of traditional anticonvulsants have been developed, for example, carbamazepine (Tegretol XR—extended release), diazepam (Diastat—rectal), fosphenytoin (Cerebyx—IM/IV), and valproate (Depacon—IV; Depakote ER—extended release). The primary advantage of these formulations may include improved adherence (fewer doses and/or better tolerability) or the availability of an injectable formulation (e.g., Depacon).

Second-Generation Anticonvulsants

The second-generation anticonvulsants include gabapentin (Neurontin), lamotrigine (Lamictal), levetiracetam (Keppra), oxcarbazepine, and topiramate (Topamax), which are used for the adjuvant treatment of partial (psychomotor) and generalized seizures. They are not currently considered superior in efficacy to the first-generation anticonvulsants in terms of seizure control. However, these agents usually do not require drug level monitoring, have fewer adverse effects (including effects on cognition), have fewer drug interactions than the first-generation anticonvulsants, and may improve adherence with once or twice daily dosing. All agents require a *slow titration period* to avoid central nervous system (CNS) adverse effects and to minimize the potential of a severe life-threatening rash (especially with lamotrigine). The second-generation anticonvulsants should be used with caution in those who are pregnant and lactating and should not be abruptly discontinued.

Refer to Table 22-1 for a summary of the anticonvulsants.

Table 22-1 Anticonvulsants

Generic Name	Trade Name	Dosage	Comments
First Generation			
carbamazepine	Tegretol	PO 400 mg–1.2 g daily in three to four divided doses, susp, tabs	For partial or generalized seizures
	Tegretol XR	PO 200–600 mg bid, ER[a] caps, tabs	Extended release; do not crush or chew
fosphenytoin	Cerebyx[b]	IV, IM, dose varies	Caution—do not confuse with Celexa (antidepressant) or Celebrex (for arthritis)
phenytoin	Dilantin	PO 200–1,200 mg daily in divided doses, IV varies, no IM	For generalized or partial seizures and status epilepticus
ethosuximide	Zarontin	PO 250 mg–1.5 g daily in divided doses	For absence seizures only
valproic acid	Depakene[c], Depakote DR[d]	PO 15–60 mg/kg daily in two to three divided doses	For absence, partial, and generalized seizures

(*Continued*)

Table 22-1 Anticonvulsants (*Continued*)

Generic Name	Trade Name	Dosage	Comments
First Generation			
	Depakote ER[a]	8%–20% higher than the daily dose of Depakote; given once daily	One dose per day; do not crush or chew
	Depacon	IV 15–60 mg/kg daily in divided doses	
Second Generation			
gabapentin	Neurontin	PO Initial dose of 300 mg tid, titrate up to 600 mg tid; higher doses may be used if tolerated	Narrow-spectrum agent with no drug interactions Max dose of 2,400 mg/day Decrease dose with renal dysfunction
lamotrigine	Lamictal	PO 100–250 mg bid (gradual titration to avoid the potential of severe skin rash)	Interactions with antiepileptic drugs mostly, hepatic and drug interaction dose adjustment needed Caution—do not confuse with Lamisil (antifungal)
levetiracetam	Keppra	PO, IV 500–3,000 mg daily divided bid	Broad-spectrum efficacy; no significant drug interactions
oxcarbazepine	Trileptal	PO 300–2,400 mg daily divided bid (renal dose adjustment may be needed)	Less significant drug interactions compared to carbamazepine; risk for hyponatremia
topiramate	Topamax	PO 50–200 mg daily bid (gradual titration; renal dose adjustment may be needed)	Interactions with antiepileptic drugs mostly; may affect cognitive function at high doses; risk of metabolic acidosis, nephrolithiasis, and weight loss

[a] Extended release.

[b] This brand name is no longer marketed, but the name is still commonly used.

[c] Regular release.

[d] Delayed release.

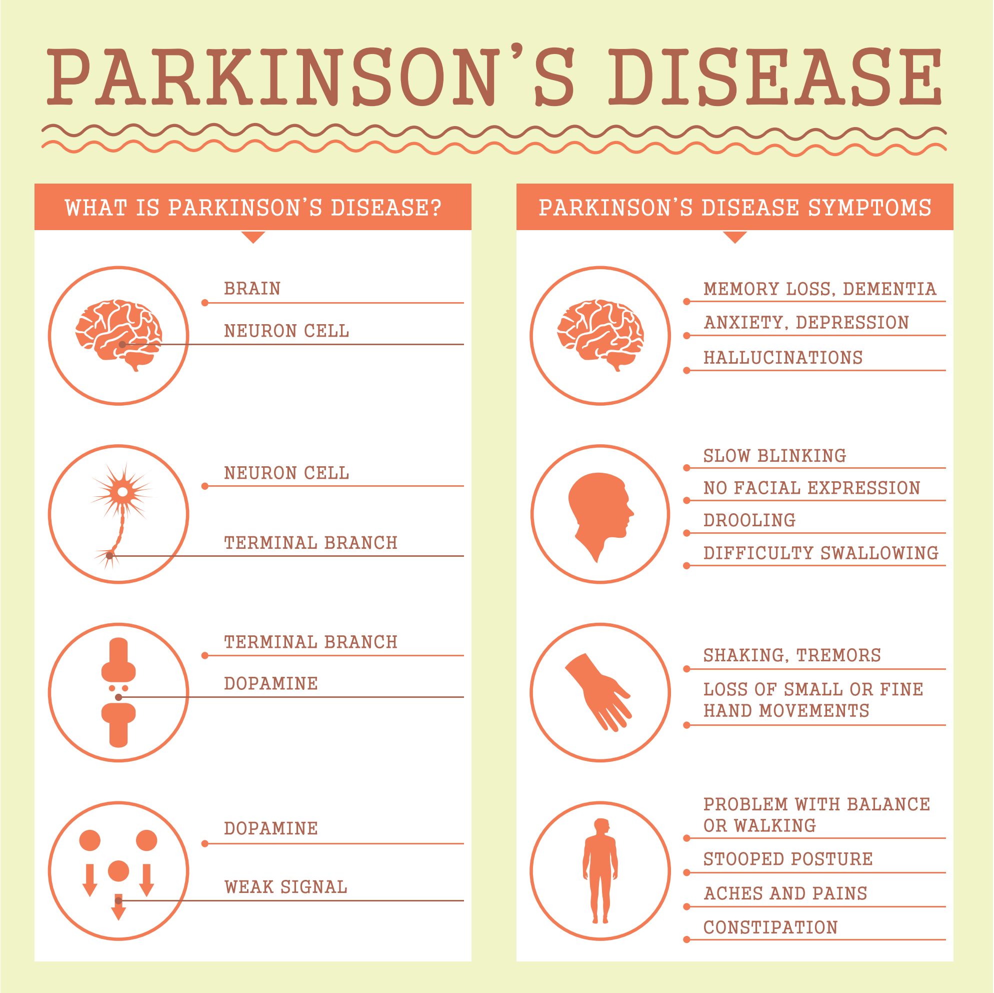
Patient Education

Patients taking any anticonvulsant medication should be instructed regarding:

- Reading the provided medication guide before they start taking an anticonvulsant and each time they get a refill
- Taking caution with driving or operating machinery until they are regulated with the medication, because of drowsiness or dizziness
- Reporting any side effects, such as rash or eye problems, staggering, slurred speech, and any other symptoms
- Ensuring careful oral hygiene until tenderness of the gums subsides as treatment progresses
- Always taking the medication on time and *never* omitting a dose (abrupt withdrawal of the medication can lead to status epilepticus)
- Wearing Medic-Alert tag or bracelet at all times in case of accident or injury
- Taking the medication with food or milk to lessen stomach upset
- Checking with the health care provider before initiating any new treatments, including OTC and herbal products (anticonvulsants are associated with numerous and potentially harmful drug–drug interactions)
- Not significantly altering the ingestion of grapefruit juice while on carbamazepine (Tegretol) because of potentiation of effect
- Parents, caregivers, and teachers should be cautioned to observe and report changes in cognitive function, mood, and behavior in children receiving anticonvulsants
- Some anticonvulsants cause an increased risk of birth defects if used during pregnancy; females of childbearing age taking anticonvulsants should be educated on using proper contraception

Antiparkinsonian Drugs

Antiparkinsonian drugs are usually given for **Parkinson's disease (PD)**, a chronic neurological disorder characterized by fine, slowly spreading muscle tremors; rigidity; and generalized slowness of movement called bradykinesia (refer to Figure 22-2). PD is one of the most common neurodegenerative diseases in adults. As the disease advances, patients develop a tendency to fall, dementia, confusion, psychosis, sleep disturbances, and declining cognitive function. Most patients with PD progress to severe disability over 10–20 years. There is no cure for Parkinson's disease, and the goal of the treatment is to relieve and slow the progression of symptoms and maintain mobility.


PARKINSON'S DISEASE
WHAT IS PARKINSON'S DISEASE?
BRAIN
NEURON CELL
NEURON CELL
TERMINAL BRANCH
TERMINAL BRANCH
DOPAMINE
DOPAMINE
WEAK SIGNAL
PARKINSON'S DISEASE SYMPTOMS
MEMORY LOSS, DEMENTIA
ANXIETY, DEPRESSION
HALLUCINATIONS
SLOW BLINKING
NO FACIAL EXPRESSION
DROOLING
DIFFICULTY SWALLOWING
SHAKING, TREMORS
LOSS OF SMALL OR FINE HAND MOVEMENTS
PROBLEM WITH BALANCE OR WALKING
STOOPED POSTURE
ACHES AND PAINS
CONSTIPATION

eveleen/Shutterstock.com.

Figure 22-2 Parkinson's disease overview.

The underlying pathology of PD is not completely understood, but normal dopamine activity as it relates to acetylcholine is diminished, and relative overactivity of cholinergic output results. This serves as the foundation of treatments for PD.

Before initiating treatment, it is important to rule out **drug-induced parkinsonism (DIP)** as a causative factor of PD. DIP is the most common form of *secondary* parkinsonism and is frequently unrecognized or misdiagnosed. Causes of DIP generally include dopamine receptor antagonists and other drugs that interfere with dopamine synthesis or release. Switching from, reducing, or discontinuing the offending agent (such as antipsychotics, calcium channel blockers, anticonvulsants, lithium, metoclopramide, or antidepressants) may be the most effective treatment option available.

Dopamine Replacement

Carbidopa–Levodopa

Levodopa crosses the blood–brain barrier, where it is converted to dopamine. Carbidopa enhances the effects of levodopa, thereby increasing the therapeutic effect of dopamine in the CNS and reducing its adverse reactions (e.g., nausea, vomiting, and low blood pressure upon standing). Sinemet (a combination of levodopa and carbidopa) is most often used for long-term treatment and is recommended as an initial drug treatment for patients with bradykinesia uncontrolled by other PD medications. As PD progresses, most patients will eventually require treatment with levodopa.

Side effects of Sinemet, which are numerous and frequent, can include:

- Dyskinesias (involuntary movements of many parts of the body)
- Nausea, vomiting, and anorexia (if given with food to prevent nausea, the protein load should be low to avoid competition for transport across the GI tract)
- Behavioral changes, anxiety, agitation, confusion, sleep disturbances, depression, hallucinations, and psychosis
- Hypotension, dizziness, and syncope

Cautions or contraindications for Sinemet apply to:

Abrupt discontinuation, which could lead to **neuroleptic malignant syndrome** (characterized by delirium, rigid muscles, fever, and autonomic nervous system instability)
Bronchial asthma or emphysema
Cardiac disease or hypotension
Active peptic ulcer
Diabetes and renal or hepatic disease
Glaucoma
Psychoses
Pregnant, postpartum, or nursing females

Interactions of Sinemet may occur with:

Antihypertensives (may potentiate hypotensive effect)
Antipsychotics (antagonistic by blocking the dopamine receptor)
Phenytoin (antagonizes levodopa)
Iron salts (reduce bioavailability)
Foods high in protein (reduce absorption)
Nonspecific (type A) monoamine oxidase inhibitors (MAOIs) (may cause hypertensive crisis)

Patients receiving Sinemet for prolonged periods of time (two to five years) may develop a tolerance, resulting in ineffectiveness of the drug called wearing off. Sometimes, changing the timing of doses, adding an extra dose at the end of the day, or adding another agent from one of the following drug classes may bring the symptoms back under control. As wearing off continues, it is not uncommon to have a patient taking Sinemet up to every 3 h, or 8× daily.

Dopamine Agonists

The newer dopamine agonists (non-ergot derivatives) pramipexole (Mirapex) and ropinirole (Requip) are commonly used in conjunction with levodopa to delay the onset of levodopa-caused motor complications or used alone in early PD or in younger patients as a "levodopa-sparing" strategy. Dopamine agonists may reduce the required dose of levodopa for patients with advanced Parkinson's. The older dopamine agonists (ergot derivatives) such as bromocriptine (Parlodel) are used much less frequently now in PD because of serious adverse effects.

Some experts recommend dopamine agonists as initial monotherapy in patients younger than 60 years. These agents have a greater specificity for dopamine receptors and may have a neuroprotective effect, which leads to less dyskinesia, may delay the *wearing-off* effect, and can postpone the need for Sinemet by several years.

Side effects of dopamine agonists are similar to those of Sinemet and can include:

- ❗ Psychosis, hallucinations, obsessive behavior, impulsivity, confusion, and somnambulism or sleepwalking (higher risk compared to Sinemet)
- ❗ Excessive sedation leading to "sleep attacks" during daily activities, including driving
- ❗ Hypotension, syncope, and peripheral edema
- ❗ Nausea and vomiting
- Pulmonary, renal, and cardiac valve fibrosis with bromocriptine
- Neuroleptic malignant syndrome with abrupt discontinuation

Interactions of dopamine agonists may occur with:

- Antidopamine agents (i.e., antipsychotics, phenothiazines, metoclopramide) may decrease the efficacy of each agent
- CNS depressants such as anxiolytics and hypnotic and sedative agents may increase the risk of somnolence

Rotigotine (Neupro patch) is a dopamine agonist applied topically with once-daily dosing. The continuous transdermal delivery of drug may be advantageous for patients who have poorly controlled PD symptoms in the early morning, slowed GI motility associated with levodopa treatment, dysphagia, or difficulty swallowing. Side effects of rotigotine are similar to other dopamine agonists, in addition to application site reactions (rotate the patch location).

MAO-B Inhibitors

Monoamine oxidase-B (MAO-B) is an enzyme responsible for breaking down dopamine and tyramine in the brain. In PD, MAO-B inhibitors will therefore increase the levels of dopamine.

Selegiline

Selegiline (Eldepryl) and *rasagiline (Azilect)* are selective MAO type-B inhibitors. Selegiline is sometimes prescribed as an adjunctive therapy for PD after levodopa has been used for several years and begins to "wear off," or become less effective. When Sinemet and selegiline or rasagiline are used *concurrently*, the Sinemet dosage is reduced by 10%–30% to lessen the chance of additive side effects. Xadago is an MAO-B inhibitor that is commonly used as adjunct therapy to carbidopa–levodopa when patients are experiencing wearing-off episodes that are not resolved by increasing dose and/or frequency.

Side effects of MAO-B inhibitors include:

Nausea, dizziness, confusion, abdominal pain, hallucinations, dry mouth, vivid dreams, dyskinesias, and headache.

Selegiline is metabolized to amphetamine metabolites, which may contribute to its side effects (especially anxiety and sleeplessness); therefore, the drug should be given no later than early afternoon.

Selegiline is **contraindicated** with the following drugs that can interact with it, resulting in rare but *severe* CNS toxicity, hyperpyrexia, hypertensive crisis, and even death. Do *not* use selegiline with:

Meperidine (Demerol), methadone, or tramadol

Tricyclic antidepressants

Selective serotonin reuptake inhibitors (SSRIs) or selective norepinephrine reuptake inhibitors (SNRIs)

Sympathomimetics (e.g., epinephrine, ephedrine, pseudoephedrine)

Dextromethorphan or St. John's wort

Abrupt discontinuation is contraindicated

When given at the recommended dosages, there is minimal danger of a hypertensive crisis associated with interactions of other MAOIs and certain foods (the "cheese reaction"). No dietary restrictions are recommended for selegiline at the recommended dose.

An orally disintegrating tablet (ODT) formulation of selegiline (Zelapar) is available as an adjunct to levodopa. Selegiline ODT is absorbed through the buccal membrane, avoiding first-pass hepatic metabolism. This results in a faster onset of action, the use of a lower dose, and fewer amphetamine metabolites.

Rasagiline

Rasagiline (Azilect) is currently the only MAO-B inhibitor approved as initial monotherapy for PD; it is also approved as an addition to levodopa later in the disease. Rasagiline is given only once daily, has no amphetamine metabolites, and is generally well tolerated. Side effects include headache, nausea, joint pain, hypotension, hallucinations, dyskinesias, depression, and dyspepsia. Contraindications are similar to selegiline.

Anticholinergic Agents

Drugs with anticholinergic and antihistaminic actions were the first to be used for tremors associated with PD and are still useful in the early stages of the disease in younger patients and for DIP. These agents restore the cholinergic–dopaminergic balance in PD. The **anticholinergics** include synthetic atropine-like drugs, such as benztropine (Cogentin) and trihexyphenidyl (Artane), which are used to treat Parkinson-like tremors associated with the long-term use of antipsychotics or for other forms of parkinsonian syndromes.

Side effects of the anticholinergic agents are:

- ❗ Dry mouth
- ❗ Dizziness and drowsiness
- ❗ Blurred vision
- Constipation or urinary retention
- ❗ Confusion
- Depression
- Nausea
- ❗ Tachycardia

Cautions or contraindications for anticholinergics apply to:

- Abrupt discontinuation (leads to rebound symptoms)
- Closed-angle glaucoma
- Use with caution in older patients because of the risk of cognitive impairment
- Those with benign prostatic hyperplasia (BPH) are also at risk for urinary retention

Amantadine

Another drug unrelated to the other antiparkinsonian agents is the antiviral agent amantadine. It alters dopamine release and has anticholinergic properties. Amantadine is used to treat parkinsonism (extrapyramidal reactions) associated with the prolonged use of phenothiazines, carbon monoxide poisoning, or cerebral arteriosclerosis in older adults. For PD, amantadine is generally used early in the disease as monotherapy, its efficacy may wane rather quickly (weeks or months), and it is of little benefit when added to levodopa.

Side effects of amantadine, usually dose related and reversible, can include:

- ❗ CNS disturbances, including depression, confusion, hallucinations, anxiety, depression, irritability, nervousness, and dizziness
- Headache, weakness, and insomnia
- ❗ Heart failure, edema, and hypotension
- ❗ GI distress, constipation, and urinary retention

Cautions or contraindications for amantadine apply to:

- Abrupt discontinuation
- Liver and kidney diseases (requires renal dose adjustment)
- Cardiac disorders
- Psychosis, neurosis, and mental depression
- Epilepsy
- Patients taking CNS drugs

COMT Inhibitors

Catechol-*O*-methyl-transferase (COMT) inhibitors, such as entacapone (Comtan) and tolcapone (Tasmar), block the enzyme responsible for metabolizing peripheral levodopa. COMT inhibitors increase the concentration of levodopa and dopamine. This allows the patient's dose of levodopa to be lowered and results in a decrease in the incidence or severity of the dose-related side effects of levodopa (e.g., dyskinesias, nausea).

Entacapone is also available in combination with carbidopa–levodopa (Stalevo), which provides the convenience of fewer pills, but dosing is less flexible for patients who need varying amounts of levodopa throughout the day. Because of the severe nature of adverse effects associated with tolcapone and extensive monitoring, it is reserved for patients who do not respond to other therapies.

Side effects of entacapone and tolcapone are similar and can include:

- ❗ Orthostatic hypotension
- ❗ Hallucinations
- ❗ Dyskinesia (levodopa dose may need to be decreased)
- Nausea and vomiting
- ❗ Diarrhea (can be severe) and abdominal pain
- Orange coloration of the urine

Hepatic injury with tolcapone (black box warning)—the treating physician is to obtain a patient-signed consent form acknowledging this risk; monitor hepatic enzymes throughout the treatment

Drug interactions: Patients taking entacapone or tolcapone should not receive *non-selective* MAOIs (phenelzine or tranylcypromine) but can take a *selective* MAOI such as selegiline. Concomitant use of CNS depressants should be avoided to prevent additive sedation.

Refer to Table 22-2 for a summary of the antiparkinsonian drugs.

Table 22-2 Antiparkinsonian Drugs

Generic Name	Trade Name	Dosage	Comments
Dopamine Replacement			
carbidopa and levodopa	Sinemet	PO 10/100–200/2,000 mg in three to six divided doses pc	Immediate release tab
	Parcopa	75 mg daily	Orally disintegrating tab
	Sinemet CR	PO 25/100–400/2,000 mg in two to four divided doses pc	Separate doses by at least 6 h
Dopamine Agonists			
bromocriptine	Parlodel	PO 1.25 mg bid with meals	Used with Sinemet; dosage gradually increased to optimum maintenance dose (up to 40 mg per day)
pramipexole	Mirapex	PO 0.125 mg tid (renal dose adjustments may be needed)	Increase to a max daily dose of 4.5 mg per day for desired effect balanced against side effects
ropinirole	Requip	PO 0.25 mg tid	Increase to a max daily dose of 24 mg per day for desired effect balanced against side effects

Generic Name	Trade Name	Dosage	Comments
rotigotine	Neupro	2–8 mg/24 h transdermally titrate upward by 2 mg per week; taper if discontinuing	Also for the treatment of restless legs syndrome
Anticholinergics			
benztropine	Cogentin	PO, IM, or IV 0.5–6 mg daily in one or divided doses	Not for older adults For drug-induced parkinsonism and other forms of parkinsonian syndrome
trihexyphenidyl	Artane[a]	PO 1–15 mg daily in divided doses	For drug-induced parkinsonism and other forms of parkinsonian syndrome
COMT Inhibitors			
entacapone	Comtan	200 mg with each dose of Sinemet (max 1,600 mg per day)	Use only with Sinemet
with carbidopa/levodopa	Stalevo	PO (various strengths) tid up to 6–8 tabs per day	Do not crush
MAO-B Inhibitors			
rasagiline	Azilect	PO 0.5–1 mg daily	Reduce dose with hepatic impairment
selegiline	Eldepryl	PO 5 mg bid (second dose no later than 2 p.m.)	Used when levodopa wears off; levodopa dosage can be decreased
	Zelapar	PO 1.25–2.5 mg daily	Orally disintegrating tablet
safinamide	Xadago	PO 50–100 mg daily	Newest MAO-B inhibitor
Other Agents			
amantadine	Symmetrel[a]	PO 100–400 mg in daily divided doses	Also for the treatment and prophylaxis of influenza A and drug-induced parkinsonism

[a] This brand name is no longer marketed, but the name is still commonly used.

Patient Education

Patients taking antiparkinsonian drugs should be instructed regarding:

- Administration on a regular schedule as prescribed, with food to lessen GI distress; give carbidopa–levodopa with a low-protein meal if food is necessary to offset nausea
- Avoiding abrupt withdrawal of the medication, which may greatly increase parkinsonian symptoms and the risk of neuroleptic malignant syndrome
- Several weeks are sometimes required before benefit is apparent
- Caution with CNS drugs, alcohol, or antihypertensives (not taking other medicines, including vitamins, without physician approval)
- Caution with driving or operation of machinery
- The fact that drugs may cause drowsiness, dizziness, or lightheadedness; with pramipexole, there may be no warning signs before falling asleep while engaged in activities of daily living
- Reporting adverse side effects to the physician (e.g., involuntary movements, blurred vision, constipation, urinary retention, GI symptoms, palpitations, and mental changes)
- With dopamine agonists, there may be intense urges to gamble or spend money, increased sexual urges, bouts of binge eating, and other intense urges
- Reporting any signs that the drug is no longer effective after prolonged use (sometimes after months or years the dosage may need to be increased or another drug may need to be substituted by the physician); avoiding any dosage changes without medical supervision
- Maintaining physical activity, self-care, and social interaction, an essential part of therapy for Parkinson's disease
- Rising slowly

Agents for Restless Legs Syndrome

Restless legs syndrome (RLS) is a sensorimotor neurologic disorder characterized by a distressing urge to move the legs, often accompanied by a marked sense of discomfort in the legs (aching, burning, pulling, itching, or tingling). RLS is triggered by rest or inactivity and is temporarily relieved by movement. It follows a circadian pattern, with symptoms being most intense in the evening and nighttime. It is usually disruptive to sleep, which is the primary reason patients seek treatment.

The etiology of RLS is either primary or secondary. Primary RLS involves the CNS and the dopaminergic pathway. The dopamine agonists pramipexole (Mirapex), ropinirole (Requip), and rotigotine (Neupro patch) used to treat PD (even though RLS is not related to PD) are FDA approved for RLS treatment as well. The dosages of the oral agents when used to treat RLS are typically only 10–20% of those used to treat PD (50% for the transdermal patch) and are usually given 1–3 h before bedtime as a single daily dose. Apply the rotigotine patch at approximately the same time every day. The most worrisome side effects with the dopamine agonists in PD, such as dyskinesias, have not been observed in patients treated for RLS.

Gabapentin (Neurontin), benzodiazepines (such as clonazepam), and opioids (hydrocodone, oxycodone, tramadol) are second-line agents for RLS cases involving specific symptoms such as continuous sleep disturbances or painful sensations in the extremities.

RLS may be secondary to other causes, including iron deficiency (with or without anemia), renal failure, diabetes, rheumatoid arthritis, fibromyalgia, vitamin deficiency (folate, B_{12}), hypothyroidism, and pregnancy. Treatment of secondary RLS focuses on identifying and treating the underlying cause. Medications that have the potential to aggravate RLS symptoms, such as metoclopramide, all neuroleptics, many antidepressants, and antihistamines, should be discontinued if possible.

Agents for Alzheimer’s Disease

Dementia is an umbrella term describing a variety of diseases and conditions that develop when nerve cells in the brain die or no longer function normally. **Alzheimer’s disease (AD),** or dementia of the Alzheimer’s type, is the most common type of dementia. It is characterized by a devastating, progressive decline in cognitive function with a gradual onset, usually beginning between 60 and 90 years of age, followed by increasingly severe impairment in social and occupational functioning. AD is ultimately fatal.

Although the precise etiology of Alzheimer’s disease is uncertain, cholinergic systems appear to be most clearly compromised and are frequently the target of current drug treatment. As AD progresses, behavioral and psychiatric symptoms are common. Nondrug interventions include trying to identify the problematic behaviors, understanding their triggers, and minimizing or eliminating those causes. These include maintaining a stable, low-stress environment; avoiding noise and glare; providing security objects; and daytime activity to improve nighttime sleep.

Cholinesterase Inhibitors

The first class of agents shown to be efficacious for the delay of symptoms in Alzheimer's disease were the cholinesterase inhibitors. These agents prevent the breakdown of acetylcholine in the synaptic cleft, thereby increasing acetylcholine levels and improving cognitive function, but they do not treat the underlying pathology of the disease. They may slow the progression, but they do not cure the disease.

Tacrine (Cognex) was the first drug approved in this class, but it was associated with significant hepatotoxicity as well a frequent dosing schedule and is no longer available. Donepezil (Aricept), galantamine (Razadyne), and rivastigmine (Exelon) are not associated with hepatotoxicity but do exhibit cholinergic side effects and dizziness. All drugs in this class cause GI upset (nausea, vomiting, diarrhea, abdominal cramps, anorexia, and weight loss), requiring slow dose titration to improve patient tolerance.

Interactions of cholinesterase inhibitors occur with:

Anticholinergics (may decrease effectiveness—avoid using together)

Cholinergics (bethanechol) and succinylcholine (may have a synergistic effect—monitor the patient closely)

Cautions or contraindications for cholinesterase inhibitors apply to:

GI bleeding and peptic ulcer disease

Cardiac disease (potential for bradycardia or syncope)

Chronic obstructive pulmonary disease (COPD; exacerbates the underlying disease)

Jaundice and renal disease

Pregnancy and lactation

Abrupt discontinuation (limit the sudden decline in cognitive function or increase in behavioral disturbances)

NMDA Receptor Antagonists

Memantine (Namenda) is the first *N*-methyl-*D*-aspartate (NMDA) antagonist approved for the treatment of moderate-to-severe dementia of the Alzheimer's type. Memantine is thought to selectively block the excitotoxic effects with abnormal transmission of the neurotransmitter glutamate. It can be used as monotherapy or in combination therapy with cholinesterase inhibitors. Memantine may be efficacious in the earlier stages of Alzheimer's disease as well, delaying the progression of symptoms and thus allowing patients to maintain certain daily functions for a little longer than they would without the drug.

Side effects of memantine involve the CNS, are dose-dependent, and include:

❗ Confusion, cerebrovascular disorder, falls, and agitation

❗ Dizziness, headache, constipation, and cough

Cautions or contraindications apply to pregnancy, lactation, use in children, and renal disease.

Drug interactions occur with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) and certain antiarrythmics.

Monoclonal Antibodies Used to Treat Alzheimer's Disease

The newest medication approved to treat Alzheimer's is lecanemab (Leqembi), which has been shown to moderately slow cognitive and functional decline in early-stage cases of the disease by reducing amyloid beta plaques, which contribute to the progression of Alzheimer's disease. Side effects, cautions, and contraindications are like those of other monoclonal antibodies and include injection site reactions, headache, and the risk of lowering the patient's ability to fight other infections.

Ultimately, the decision on whether to continue drug therapy in Alzheimer's patients is based on quality of life, treatment goals, potential benefits, adverse effects, and costs. If their quality of life is poor, stabilizing or slowing further decline may not be an appropriate goal, and drug therapy should be discontinued.

Refer to Table 22-3 for a summary of Alzheimer's drugs.

Table 22-3 Agents for Alzheimer's Disease (AD)

Generic Name	Trade Name	Dosage	Comments
Cholinesterase Inhibitors			
donepezil	Aricept	PO 5 mg at bedtime, increase to 10 mg after 4 to 6 weeks, up to 23 mg	5 mg for mild to moderate AD; 10 mg for mild, moderate, and severe AD; 23 mg for moderate to severe AD
	Aricept ODT	5 mg daily	Orally disintegrating tablet
rivastigmine	Exelon	PO 1.5 mg bid with food Patch 4.6 mg per 24 h; titrate to 9.5 mg per 24 h after 4 weeks	Increase to 3–6 mg bid (higher doses may be more beneficial) Rotate application sites; can increase up to max effective dose of 13.3 mg per 24 h
galantamine	Razadyne[a]	PO 4–12 mg bid with food	Caution with hepatic or renal disease
	Razadyne ER	PO 8 mg daily with food	Titrate to 16–24 mg once daily; do not crush
NMDA Receptor Antagonists			
memantine	Namenda	PO 5 mg per day initially; titrate to 10 mg bid over 4 weeks	Can be used as monotherapy or in combination therapy with cholinesterase inhibitors CNS side effects, especially agitation
	Namenda XR	PO 7 mg per day initially; titrate to 28 mg once daily over 4 weeks	Do not crush or chew; may open capsule and sprinkle contents on applesauce before swallowing
Monoclonal Antibodies Used to Treat Alzheimer's			
lecanemab	Leqembi	IV 10 mg/kg every 2 weeks	Discontinue if Alzheimer's symptoms become severe

[a] Formerly Reminyl.

Case Study A

Anticonvulsant Drugs

While standing in line with a friend at a local coffee shop, a person abruptly loses consciousness and falls to the ground. For the next 2 min, they experience alternating contraction and relaxation of their extremities. Their friend instructs the coffee shop cashier to call 911 to report that a customer is having a seizure.

1. What type of seizure is the person experiencing?
- a. Atypical
- b. Generalized
- c. Febrile
- d. Partial

2. After the person is taken to the emergency department and treated by a neurologist, they are prescribed carbamazepine. The nurse explains that the patient might experience what side effect from the drug?
- a. Hypernatremia
- b. Gingivitis
- c. Ataxia
- d. Headache

3. The nurse also cautions the patient that carbamazepine has multiple interactions with other substances. Which of the following should the patient avoid because it can potentiate the effect of carbamazepine?
- a. Rifampin
- b. Phenobarbital
- c. Green tea
- d. Grapefruit juice

4. Which category of drug can increase the levels of carbamazepine?
- a. Calcium channel blockers
- b. Antidiarrheals
- c. Anticoagulants
- d. Antacids

5. The patient is concerned about their quality of daily life while taking carbamazepine. What can the nurse explain as an advantage of taking carbamazepine for seizure control?
- a. No liver or kidney complications
- b. Minimal sedation and cognitive effects
- c. No cardiac complications
- d. Can be taken while pregnant

Case Study B

A patient is at the neurologist's office to receive the results of recent testing after their complaint of muscle tremors, rigidity, and slow movement.

1. The physician explains that the patient has Parkinson's disease (PD), a chronic neurological disease characterized by:
- a. Akathesia
- b. Tardive dyskinesia
- c. Myocutaneous tightening
- d. Bradykinesia

2. The neurologist prescribes an antiparkinsonian drug, Sinemet, and instructs the patient on which of the following?
- a. The drug may cause increased wakefulness.
- b. Expect to see the benefits of the drug in 3 to 5 days.
- c. Take the drug with a small nonprotein snack to lessen GI distress.
- d. Stop taking the drug immediately if feeling side effects.

3. The physician also explains to the patient that caution should be exercised when they get up to walk. This is because Sinemet can cause which side effect?
- a. Seizures
- b. Hypotension
- c. Blurred vision
- d. Muscular weakness

(*Continued*)

4. An abrupt discontinuation of Sinemet can lead to which complication?
a. Myocardial infarction
b. Severe shortness of breath
c. Hypoglycemia
d. Neuroleptic malignant syndrome

5. An interaction of Sinemet may occur with:
a. Antihypertensives
b. Multivitamins
c. Antidepressants
d. Foods high in carbohydrates

Chapter Review Quiz

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication

1. ______ Aricept
2. ______ entacapone
3. ______ Neurontin
4. ______ Lamictal
5. ______ Zarontin
6. ______ amantadine
7. ______ Depakote
8. ______ Cogentin
9. ______ Topamax
10. ______ Razadyne

Condition

a. Seizures
b. Absence seizure
c. Parkinson's disease
d. Extrapyramidal reactions
e. Alzheimer's disease

Choose the correct answer

11. A common side effect of phenytoin is:
a. Hypertension
b. Muscle cramps
c. Sedation
d. Dehydration

12. Health care professionals should closely monitor patients receiving anticonvulsants for which condition?
a. Hyperactivity
b. Mania
c. Insomnia
d. Suicidal ideation

13. Which of the following can interact with carbamazepine (Tegretol), potentiating the risk of side effects?
a. Dairy products
b. Grapefruit juice
c. Aspirin
d. Iron

14. Anticholinergics used to treat younger patients with PD may cause which side effect?

a. Drooling
b. Night sweats
c. Dry mouth
d. Bradycardia

15. Caution should be used when administering memantine to patients with Alzheimer's disease because there is an increased risk of:

a. Diabetic ketoacidosis
b. Falls
c. Nausea and vomiting
d. Decreased gag reflex

16. Patients taking any anticonvulsant medication should be instructed to:

a. Take the medication with food
b. Expect slurred speech with the first dose
c. Omit a dose if experiencing nausea
d. Perform vigorous dental hygiene

17. Most children who experience febrile seizures do not require anticonvulsant drug therapy.

a. True
b. False

18. Which of the following is not a first-line therapy for restless leg syndrome (RLS)?

a. Pramipexole (Mirapex)
b. Ropinirole (Requip)
c. Rotigotine (Neupro patch)
d. Gabapentin (Neurotin)

Chapter 23

Endocrine System Drugs

Key Terms and Concepts

Antidiabetic
Antithyroid
Corticosteroids
Endocrine
Hormones
Hyperglycemia
Hypoglycemia
Hyperthyroidism
Hypothyroidism
Sulfonylureas

Objectives

Upon completion of this chapter, the learner should be able to:

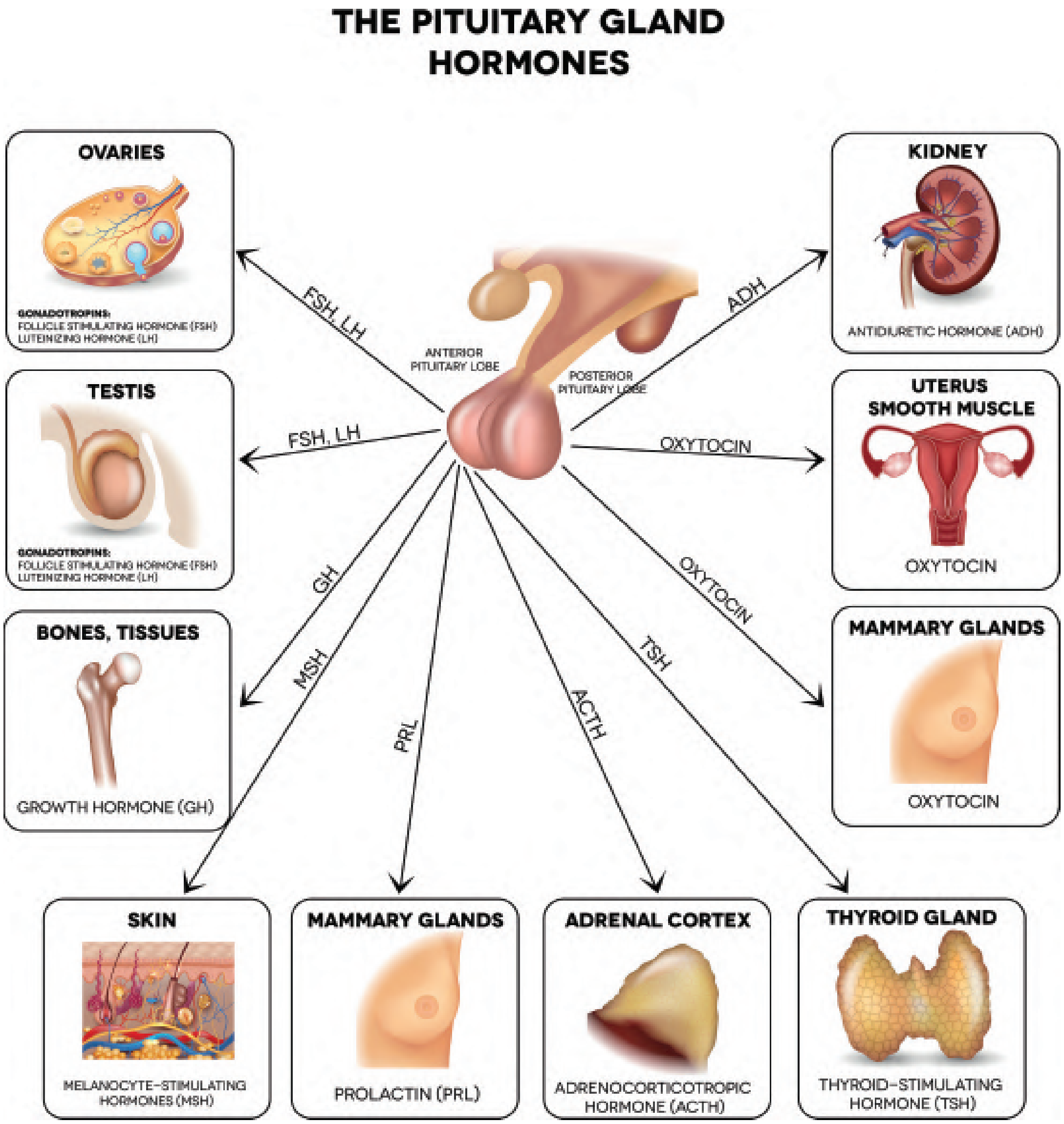
1. Identify the hormones secreted by these four endocrine glands: pituitary, adrenals, thyroid, and pancreas.
2. Describe the various conditions that can be treated with corticosteroids.
3. Explain the proper administration of corticosteroid therapy.
4. List serious potential side effects of long-term steroid therapy.
5. Describe medications given for hypothyroidism and hyperthyroidism and their side effects.
6. Identify the symptoms of hypoglycemia and hyperglycemia and appropriate interventions.
7. Explain the uses and side effects of oral and injectable noninsulin antidiabetics.
8. Compare and contrast insulins according to their action (rapid, intermediate, and long-acting), naming the onset, peak, and duration of each category.

The **endocrine** system, much like the nervous system, is a body control system. Unlike the nervous system, it often exerts its effects more slowly and over a longer period of time. *Endo* means "within," and *endocrine* refers to an internal secretion of *hormones* produced by a ductless gland that secretes directly into the bloodstream. **Hormones** are chemical messengers that have specialized functions in regulating the activities of specific cells or organs as they travel though the bloodstream to their targets. Endocrine system drugs include natural hormones secreted by the ductless glands as well as synthetic substitutes. This chapter covers four categories: pituitary hormones, adrenal corticosteroids, thyroid agents, and antidiabetic agents.

Pituitary Hormones

The pituitary gland, located at the base of the brain, regulates the function of the other glands. Please refer to Figure 23-1. It secretes several hormones, including somatotropin, adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and gonadotropic hormones (FSH, LH, and LTH). The two pituitary hormones discussed in this chapter are somatotropin and ACTH.

The anterior pituitary lobe hormone, somatotropin, is called human growth hormone (HGH) because it regulates growth. Insufficient production of HGH will result in growth abnormalities, which should be treated only by an endocrinologist.


THE PITUITARY GLAND
HORMONES
OVARIES
GONADOTROPINS:
FOLLICLE STIMULATING HORMONE (FSH)
LUTEINIZING HORMONE (LH)
TESTIS
GONADOTROPINS:
FOLLICLE STIMULATING HORMONE (FSH)
LUTEINIZING HORMONE (LH)
BONES, TISSUES
GROWTH HORMONE (GH)
KIDNEY
ANTIDIURETIC HORMONE (ADH)
UTERUS
SMOOTH MUSCLE
OXYTOCIN
MAMMARY GLANDS
OXYTOCIN
ANTERIOR
PITUITARY LOBE
POSTERIOR
PITUITARY LOBE
FSH, LH
FSH, LH
GH
MSH
PRL
ACTH
TSH
OXYTOCIN
OXYTOCIN
ADH
SKIN
MELANOCYTE-STIMULATING
HORMONES (MSH)
MAMMARY GLANDS
PROLACTIN (PRL)
ADRENAL CORTEX
ADRENOCORTICOTROPIC
HORMONE (ACTH)
THYROID GLAND
THYROID-STIMULATING
HORMONE (TSH)

iStock.com/TefiM.

Figure 23-1 While all signaling hormones and target glands are not discussed in this chapter, this figure displays the importance and wide range of effects that the pituitary gland has in the body.

Adrenocorticotropic hormone (ACTH) is available only for parenteral use as corticotropin. Cosyntropin (Cortrosyn), a synthetic peptide of ACTH, is used mainly for the diagnosis of adrenocortical insufficiency. Treatment of associated disorders is usually reserved for the corticosteroids, where the dosage is more easily regulated and for which oral forms are available as well.

Adrenal Corticosteroids

The adrenal glands, located adjacent to the kidneys, secrete hormones called **corticosteroids**, which act on the immune system to *suppress the body's response to infection or trauma.* They *relieve inflammation, reduce swelling,* and *suppress symptoms* in acute conditions. Corticosteroid use can be subdivided into two broad categories: (1) as replacement therapy when secretions of the pituitary or adrenal glands are deficient (e.g., for Addison's disease) and (2) as anti-inflammatory and immunosuppressant agents.

Corticosteroid therapy is *not curative* but is used as *supportive therapy with other medications.* Some conditions treated with corticosteroids include:

Allergic reactions (e.g., to insect bites, poison plants, chemicals, or other medications) in which there are symptoms of rash, hives, or anaphylaxis

Acute flare-ups of rheumatic or collagen disorders, especially where only a few inflamed joints can be injected with corticosteroids to decrease crippling conditions or in life-threatening situations, such as rheumatic carditis or lupus

Acute flare-ups of severe skin conditions that do not respond to conservative therapy; topical applications are preferable to systemic therapy, when possible, to minimize side effects

Acute respiratory disorders such as status asthmaticus (persistent and intractable asthma) (intravenous preparations are preferable) and sarcoidosis or to prevent hyaline membrane disease in premature infants by administering IM to the patient who is pregnant at least 24 h before delivery

Long-term prevention of symptoms in severe persistent asthma, for which corticosteroids are used for long-term symptom prevention, or COPD, for which corticosteroids are used for chronic [long-term] symptom management at the lowest possible effective dose (oral inhalations are preferable for both conditions).

Malignancies (e.g., leukemia, lymphoma, and Hodgkin's disease), in which corticosteroids (e.g., prednisone) are used with other antineoplastic drugs as part of the chemotherapy regimen; treatment of nausea and vomiting associated with chemotherapy (e.g., dexamethasone)

Cerebral edema associated with brain tumor or neurosurgery

Organ transplant, in which corticosteroids are used with other immunosuppressive drugs to prevent the rejection of transplanted organs

Life-threatening shock owing to adrenocortical insufficiency; treatment of other forms of shock is controversial

Acute flare-ups of ulcerative colitis; short-term use only to avoid hemorrhage

Prolonged administration of corticosteroids can cause suppression of the pituitary gland with adrenocortical atrophy, in which the body no longer produces its own hormones. To minimize this effect, intermediate-acting corticosteroids (prednisone, methylprednisolone) can be given by alternate-day therapy when they are required for extended time periods. Withdrawal of corticosteroids following long-term therapy should always be gradual, with step-down (i.e., tapering) dosage to allow the body's normal hormone production and regulation to return. This is especially important with patients whose therapy exceeds 14 consecutive days at a dose of 20 mg of prednisone (or equivalent) per day or more. Abrupt withdrawal can lead to acute adrenal insufficiency, shock, and even death.

Because of the potentially serious side effects, corticosteroids are administered for as short a time as possible and *locally if possible* to reduce systemic effects (e.g., in ointment, intra-articular injections, ophthalmic drops, and respiratory aerosol inhalants). Local administration reduces the dosage by avoiding the first-pass effect and going directly to the site of need. For *acute* episodes, some oral corticosteroids are available in *dose packs* (e.g., Medrol Dosepak, prednisone pak, DexPak TaperPak) to facilitate dose tapering.

Side effects of corticosteroids used for longer than very brief periods can be quite serious and possibly include:

- Adrenocortical insufficiency and adrenocortical atrophy
- ❗ Delayed wound healing and *increased susceptibility to infection*
- Fluid and electrolyte imbalance, possibly resulting in edema, potassium loss, hypertension, and heart failure
- ❗ Muscle pain or weakness
- ❗ Osteoporosis with fractures, especially in older adult females
- ❗ Stunting of growth in children (premature closure of bone ends)
- Increased intraocular pressure or cataracts
- ❗ Cushing's syndrome, including obesity of the trunk, "moon face," acne, hirsutism), amenorrhea, and *hyperglycemia*
- ❗ *Gastric* or esophageal irritation, ulceration, or hemorrhage
- ❗ CNS effects, including headache, vertigo, insomnia, euphoria, psychosis, or anxiety
- ❗ Petechiae, easy bruising, and skin thinning and tearing
- ❗ Increased blood sugar or fluctuating blood sugar levels (counsel patients who test blood sugar regularly)

Cautions or contraindications apply to:

- Long-term use (regulated carefully; avoid abrupt discontinuation)
- Viral or bacterial infections (used only in life-threatening situations along with appropriate anti-infectives)
- Fungal infections (only if specific therapy is concurrent)
- Hypothyroidism or cirrhosis (exaggerated response to corticosteroids)
- Hypertension or heart failure

Patients with psychosis or emotional instability
Diabetes (drugs increase hyperglycemia)
Glaucoma (drugs may increase intraocular pressure)
Cataracts (cause or worsening of cataracts)
History of gastric or esophageal irritation (may precipitate ulcers)
Children (drugs may delay growth)
Pregnancy and lactation
History of thromboembolic disorders or seizures

Interactions may occur with:

Barbiturates, phenytoin (Dilantin), and rifampin (may reduce the effectiveness of corticosteroids)
Estrogen and oral contraceptives (may potentiate corticosteroids)
Nonsteroidal anti-inflammatory agents or salicylates (e.g., aspirin may increase the risk of gastrointestinal [GI] ulceration)
Diuretics (potentiate potassium depletion, e.g., thiazides and furosemide)
Live-virus vaccines and toxoids (long-term or high-dose corticosteroids inhibit the antibody response)
Bupropion (dose-related risk of seizures)
Haloperidol (increased risk of QT prolongation)

Refer to Table 23-1 for a summary of the pituitary and adrenal corticosteroids.

Table 23-1 Pituitary and Adrenal Corticosteroid Drugs

Generic Name	Trade Name	Dosage
Pituitary Drugs		
corticotropin (ACTH)	H. P. Acthar Gel	IM, SQ repository gel for injection
cosyntropin	Cortrosyn	IM and IV for adrenocortical insufficiency diagnosis
Adrenal Corticosteroids[a]		
cortisone		PO for replacement
dexamethasone	Decadron[b]	PO, IV, IM
fludrocortisone	Florinef[b]	PO, for orthostatic hypotension
hydrocortisone	Cortef or Solu-Cortef	PO, IV, deep IM, SQ
methylprednisolone	Medrol, Depo-Medrol, or Solu-Medrol	PO, IV, deep IM, intra-articular
prednisone	Sterapred	PO (tab or liquid); do not confuse with prednisolone
triamcinolone	Kenalog	IM, intra-articular (never IV)

Note: Many other products are available. This is a representative list.

[a] Dosage varies greatly depending on the condition treated; large doses may be given for acute conditions on a short-term basis; long-term therapy can be given on an alternate-day basis with intermediate-acting agents, and dosage is reduced gradually to the lowest possible effective dose.

[b] This brand name is no longer marketed, but the name is still commonly used.

Patient Education

Patients taking corticosteroids should be instructed regarding:

Following exact dosage and administration orders (never taking longer than indicated and never stopping medicine abruptly)

Notifying the physician of any signs of infection or trauma *while taking corticosteroids or within 12 months after long-term therapy is discontinued* and similarly notifying the surgeon, dentist, or anesthesiologist if required

Taking oral corticosteroids during or immediately after meals or with milk to decrease gastric irritation

Taking single daily or alternate-day doses prior to 9 a.m.; taking multiple doses at evenly spaced intervals throughout the day but not near bedtime

Avoiding any other drugs at the same time (including over-the-counter [OTC] drugs, e.g., aspirin) without the physician's approval (antacids or other antiulcer drugs are sometimes prescribed)

Side effects to expect with the long-term therapy (e.g., fluid retention and edema)

Dangers of infection, delayed wound healing, osteoporosis, and mental health disorders

Reporting any side effects to the physician immediately

Thyroid Disorders

The thyroid is an endocrine gland located in the front part of the neck and is responsible for regulating the rate of metabolism. When thyroid levels are low, the pituitary gland releases TSH. TSH promotes the biosynthesis and secretion of the two bioactive thyroid hormones thyroxine (T4) and triiodothyronine (T3, the active form of thyroid hormone). Thyroxine is the major product of the thyroid gland, and much of it is later converted in the body to the active T3 form.

Thyroid Agents

Thyroid agents can be natural (thyroid) or synthetic (e.g., Synthroid). Thyroid preparations are used in replacement therapy for **hypothyroidism**, the most common thyroid problem in the United States, which is caused by diminished or absent thyroid function. Synthetic agents, such as levothyroxine (Levoxyl), are generally preferred because T4 is a prohormone, and this allows the patient's own physiological mechanisms to control the production of T3. Refer to Figure 23-2 for common symptoms of hypothyroidism.

Hypothyroid conditions requiring replacement therapy include *cretinism* (congenital; requires immediate treatment to prevent intellectual disabilities) and *myxedema* or adult hypothyroidism owing to simple goiter, Hashimoto's thyroiditis, pituitary disorders, medications (amiodarone, lithium), and thyroid destruction from surgery or radiation. Hypothyroidism causes slowed metabolism with symptoms ranging from fatigue, somnolence, dry skin, thinning hair, weight gain, constipation, sensitivity to cold, and irregular menses to mental deterioration (including depression) if untreated.

Note

The use of thyroid agents in weight reduction programs to increase metabolism when thyroid function is normal (euthyroid) is *contraindicated*, ineffective, and dangerous, leading to a decrease in normal thyroid function and possibly life-threatening cardiac arrhythmias.

Transient hypothyroidism is rare, and thyroid replacement therapy for true hypothyroidism must be continued for life, although dosage adjustments may be required. Monitoring for toxic effects and periodic laboratory tests are recommended. Most patients are started on 100–125 mcg of levothyroxine as an initial dose. This starting value can vary based on severity of symptoms, TSH levels, and weight and body composition. Dosing adjustments are based on patient reported symptoms for hyper- or hypothyroidism, as well as TSH levels that are generally drawn every 4 to 6 weeks until the dosage is stabilized.

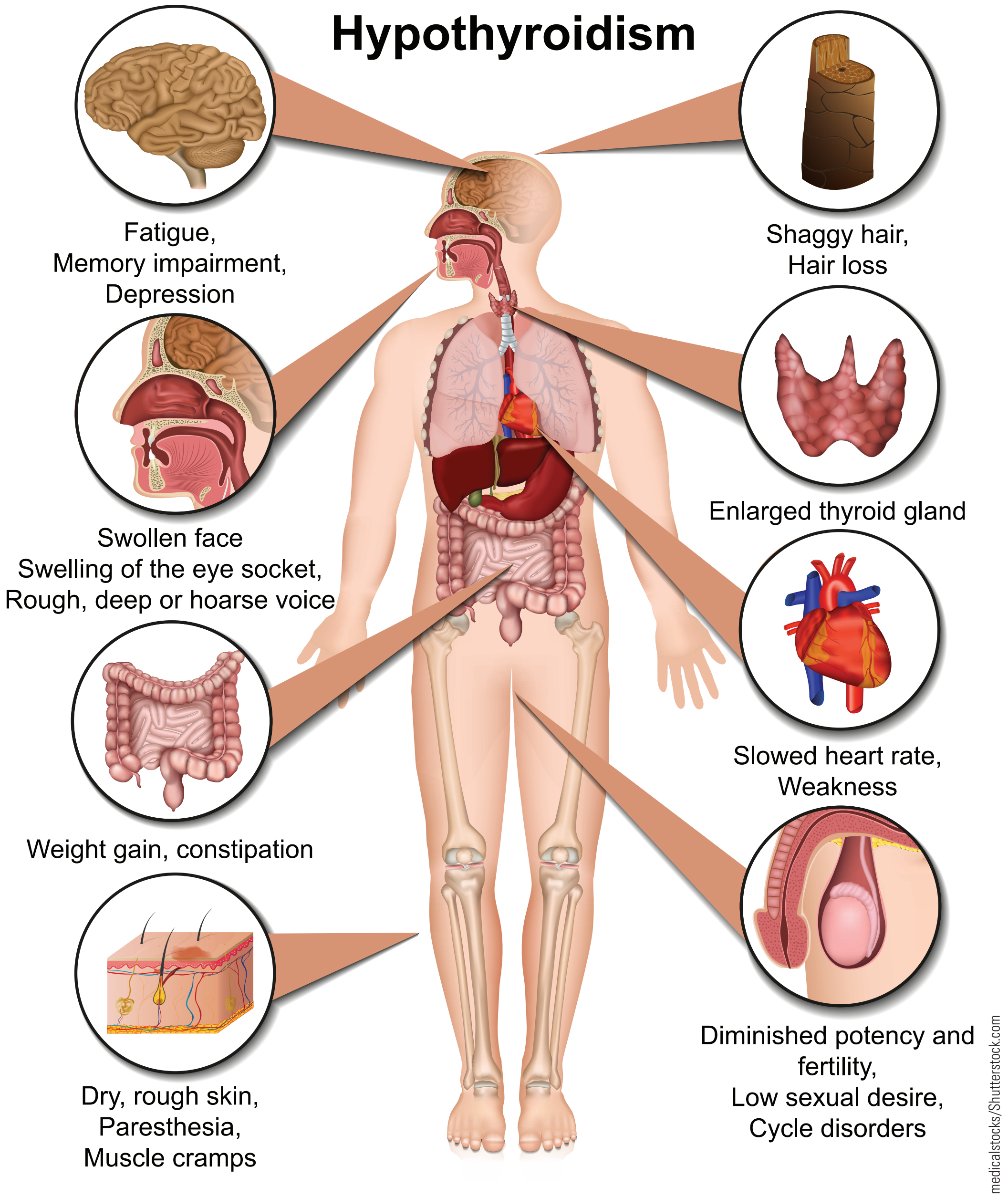

Hypothyroidism
Fatigue,
Memory impairment,
Depression
Shaggy hair,
Hair loss
Swollen face
Swelling of the eye socket,
Rough, deep or hoarse voice
Enlarged thyroid gland
Weight gain, constipation
Slowed heart rate,
Weakness
Dry, rough skin,
Paresthesia,
Muscle cramps
Diminished potency and
fertility,
Low sexual desire,
Cycle disorders
medicalstocks/Shutterstock.com

Figure 23-2 Hypothyroid disorders can present with symptoms that manifest throughout the body.

Toxic effects are the result of overdosage of thyroid hormones and are manifested in the signs of *hyperthyroidism*:

Palpitations, chest pain, tachycardia, cardiac arrhythmias, and increased blood pressure

Nervousness, difficulty concentrating, tremor, muscle weakness, headache, and insomnia

Weight loss (in spite of increased appetite), diarrhea, and abdominal cramps

Intolerance to heat, fever, and excessive sweating; easy fatigability

Menstrual irregularities; exophthalmos (bulging eyes)

Cautions or contraindications for thyroid hormones apply to:

Cardiovascular disease, including angina pectoris, myocardial infarction, and hypertension

Older adults (may precipitate dormant cardiac pathology)

Adrenal insufficiency (corticosteroids are required first)

Diabetes (close monitoring of blood glucose is required)

Interactions of thyroid hormones may occur with:

Food (can diminish absorption by 50%)—take on an empty stomach

Potentiation of oral anticoagulant effects if added after warfarin therapy is stabilized

Insulin and oral hypoglycemics (dosage adjustment is necessary)

Potentiation of adrenergic effect (e.g., epinephrine; monitor closely!)

Estrogens and oral contraceptives (decreased thyroid response)

Amiodarone (contains about 37% iodine by weight but can cause either hypo- or hyperthyroidism; monitor for changes in thyroid function)

Aluminum/calcium/iron/magnesium salts, chromium, and sucralfate (decreased absorption; space several hours apart if possible)

Soy products (decreased response)

Patient Education

Patients being treated with thyroid medication should be instructed regarding:

Importance of taking the prescribed dosage of the thyroid medication consistently every day; it usually has to be taken for life; **take on empty stomach 30–60 min prior to breakfast**

Importance of reporting any symptoms of overdose (e.g., palpitations, nervousness, excessive sweating, and unexplained weight loss)

Periodic laboratory tests to determine the effectiveness and proper dosage

Not changing from one brand to another or to a generic form without physician approval (if switched, TSH should be retested in 6 weeks)

Clinical Application

Narrow Therapeutic Index Drugs

Some medications are classified as narrow therapeutic index (NTI) drugs. This means that the range for therapeutic effect is very small, where a small increase in dosage could lead to an overdose (side effects), or a small decrease in dosage could lead to subtherapeutic effects. Because of this, these drugs are often dosed in micrograms rather than milligrams, which allows for more precise dosing for these often potent medications. Patients taking NTI drugs often require laboratory monitoring to ensure that the desired drug levels are achieved. Levothyroxine (Synthroid) is one example of an NTI drug. Special care must be taken with NTI drugs, as an incorrect dose could have extreme effects. For example, patients are instructed to take levothyroxine on an empty stomach; if they do not do this regularly, the absorption of the drug can vary greatly. Therefore, it is important to counsel patients to take the drugs exactly as prescribed, and to double-check all doses upon dispensing or administering NTI drugs.

Antithyroid Agents

Hyperthyroidism can be caused by Graves' disease (an autoimmune disorder where antibodies mistakenly attack the thyroid gland) and thyroiditis (inflammation of the thyroid gland). Orally administered radioactive iodine ablation (destruction) therapy is the most common treatment, and most patients are cured after a single dose. Surgery to remove all or part of the diseased thyroid is another permanent cure for hyperthyroidism, but this is seldom used now. The cure for hyperthyroidism is the destruction or removal of the gland, resulting in hypothyroidism. The result is that most people with hyperthyroidism end up needing lifelong hypothyroid treatment. Refer to Figure 23-3.

Antithyroid agents (e.g., methimazole [Tapazole] and propylthiouracil [PTU]) are used *to relieve the symptoms of hyperthyroidism* in preparation for surgical or radioactive iodine therapy or for those who are not candidates for either procedure. Methimazole is generally considered the treatment of choice because it works more quickly and is less likely to cause liver injury than PTU. Antithyroid drugs are not helpful for the treatment of hyperthyroidism associated with thyroiditis because this condition is due to the release, not the overproduction, of thyroid hormones.

Side effects of antithyroid agents are rare and may include:

Rash, urticaria, and pruritus (treat with antihistamines)
Abnormal sense of taste
Blood dyscrasias (especially agranulocytosis)

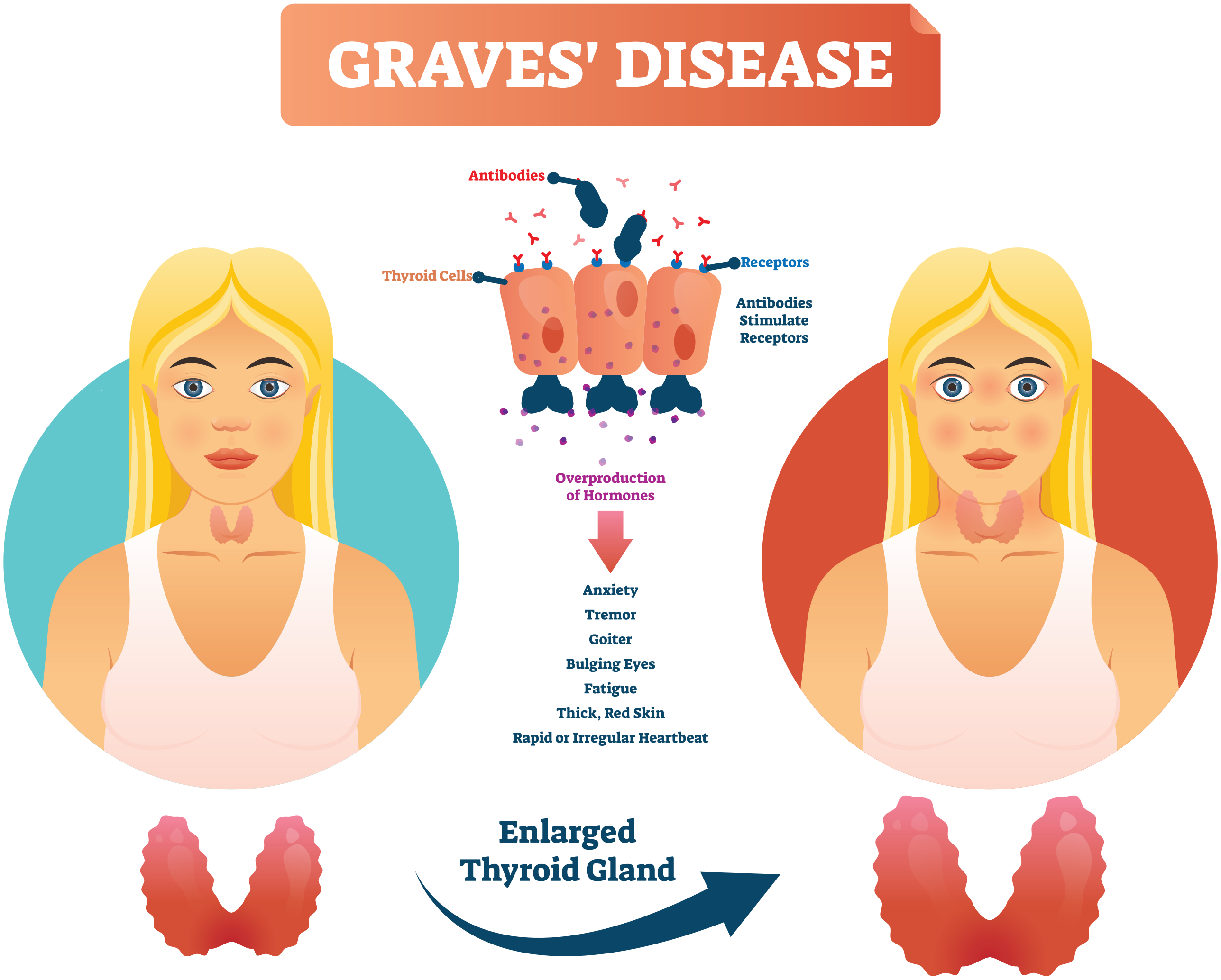
Cautions or contraindications for antithyroid agents apply to:

Prolonged therapy (seldom used)
Patients older than 40 years
Pregnancy and lactation
Hepatic disorders (black box warning with PTU)

Interactions occur with:

Other drugs causing agranulocytosis (they are potentiated)

Excessive iodine intake or drugs containing iodine, such as amiodarone (decreased efficacy)


GRAVES' DISEASE
Antibodies
Thyroid Cells
Receptors
Antibodies Stimulate Receptors
Overproduction of Hormones
Anxiety
Tremor
Goiter
Bulging Eyes
Fatigue
Thick, Red Skin
Rapid or Irregular Heartbeat
Enlarged Thyroid Gland

VectorMine/Shutterstock.com

Figure 23-3 Graves' disease (hyperthyroid) can present with symptoms that manifest throughout the body.

Patient Education

Patients being treated with antithyroid medication should be instructed to:

Take doses at regular intervals

Notify the physician immediately of signs of illness (e.g., chills, fever, rash, sore throat, malaise, and jaundice)

Refer to Table 23-2 for a summary of thyroid and antithyroid agents.

Table 23-2 Thyroid and Antithyroid Agents

Generic Name	Trade Name	Dosage
Thyroid Agents		
levothyroxine (T4)	Synthroid, Levothroid, Levoxyl	PO, 25–300 mcg daily[a] IV, 50% of PO dose initially
liothyronine (T3)	Cytomel	PO 5–25 mcg daily
thyroid (T3 & T4)	Armour Thyroid	PO 60–180 mg daily
Antithyroid Agents		
methimazole	Tapazole	Tabs, PO 5–40 mg daily, in divided doses
propylthiouracil	PTU	Tabs, PO 100–400 mg daily in divided doses

[a] When receiving orders for levothyroxine, caution is advised about decimal point placement (i.e., 0.025 mg vs. 0.25 mg) and dose conversions between mg and mcg, as medication errors have occurred.

Antidiabetic Agents

Diabetes mellitus (DM) makes up a group of hormonal diseases characterized by impaired metabolism of carbohydrates, fats, and proteins, resulting in elevated levels of blood glucose. Diabetes is one of the most prevalent and costly diseases in America, affecting almost 39 million Americans, around 12% of the population, with many more people at the prediabetic stage or not even knowing that they have the disease. Prediabetes is a condition where blood glucose levels are higher than normal but not high enough to be called diabetes. Often, prediabetes is treated with metformin (discussed later in this chapter), to help slow/prevent a diabetes diagnosis.

DM is classified as insulin-dependent type 1 (characterized by the destruction of pancreatic beta cells) or type 2 (characterized by insulin resistance and deficiency). Type 1 diabetes was formerly described as juvenile diabetes because it was usually diagnosed in children and young adults. However, older adults can also develop type 1 diabetes. Regardless of age, DM type 1 will require insulin therapy. Type 2 diabetes is the most common (90–95%) form of diabetes. There has been an increase in children and young adults with type 2 because of an increase in the rate of obesity at an earlier age.

Whereas type 1 diabetes results from a genetic or clinical destruction of pancreatic beta cells, type 2 results from a loss of sensitivity to insulin, which results from genetics or lifestyle (diet, exercise, etc.) or a combination of the two. Differences between the two disease states are outlined in Table 23-3.

The result of long-term, poorly controlled diabetes is vascular injury, which is categorized as microvascular or macrovascular. Common microvascular complications include retinopathy, nephropathy, and neuropathy. Common macrovascular complications of diabetes include coronary artery disease (including myocardial infarction), cerebrovascular disease (including stroke), and peripheral vascular disease. DM is considered to be the seventh leading cause of death in the United States; about 70% of patients with diabetes die of heart disease or stroke and a person with diabetes is twice as likely to experience one of these events as a person without diabetes. Health professionals of all disciplines have a responsibility to care for each patient in such a way that the risk of diabetic complications is minimized. DM can cause complications with the eyes, extremities (especially feet), skin, nails, and teeth, which is why medical professionals from all specialties need to be familiar with diabetes.

Medications that are administered to *lower blood glucose levels* include parenteral insulin and oral and injectable noninsulin **antidiabetic** agents.

Table 23-3 Diabetes Type I vs. Type II

Characteristic	Type I	Type II
Age	Young (usually less than 35 years)	Older
Onset	Rapid (ketoacidosis)	Gradual, with no symptoms in early stages
Body composition	non-obese	Obese
Cause	Body cannot produce insulin	Insulin production is normal or altered to some degree; body cells are resistant to insulin
Management	Insulin injections with diet and exercise	Oral/injectable noninsulin medications with insulin injections only if needed; diet and exercise

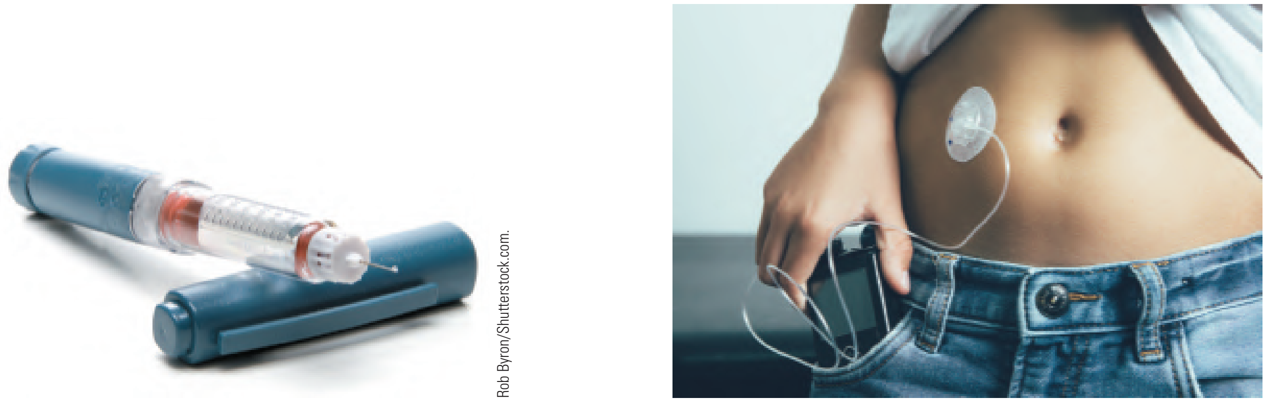
Insulin

Insulin is required as replacement therapy for patients with type 1 diabetes with insufficient production of insulin from the islets of Langerhans in the pancreas. Insulin is also required in patients with type 2 diabetes who have failed to maintain satisfactory concentrations of blood glucose with therapy including dietary regulation and oral antidiabetic agents. Insulin is rarely used as first-line therapy for type 2 diabetes. Insulin is also indicated for patients with stable type 2 diabetes at the time of surgery, fever, severe trauma, infection, serious renal or hepatic dysfunction, endocrine dysfunction, gangrene, or pregnancy. Insulin (regular) is used in the emergency treatment of diabetic ketoacidosis or coma.

Insulin is most commonly administered parenterally because it is easily destroyed in the GI tract. Newer inhaled insulin preparations are currently being researched but are not used as frequently as injectable formulations. All *injected* insulin products currently marketed are one of two types: biosynthetic human or analog. Biosynthetic insulins are referred to as "human" because their amino acid structure is identical to that of naturally occurring human insulin. Analog insulin (aspart, detemir, glargine, glulisine, and lispro), which mimics normal insulin secretion better than traditional insulins and reduces hypoglycemia, differs from human insulin only by substitution or position changes in the human insulin molecule. Biosynthetic and analog insulins are created using recombinant DNA technology.

Most of the insulin used today is U-100, which means that there are 100 units of insulin in each milliliter. The insulin syringe *must be marked U-100* to match the insulin used. Remember that on the 100-unit (1-mL) insulin syringe, each line represents 2 units. If a smaller 50-unit (1/2-mL) syringe is used, each line represents 1 unit of insulin. *To prevent errors—which could have serious consequences—always* *have a clinician compare the insulin in the syringe with the dosage ordered*. Some insulin is available in U-200 and U-500, which means that there are 200 and 500 units, respectively, in each milliliter. These formulations are reserved for patients who require very large doses of insulin. Extra care should be taken when administering these formulations to patients, and special counseling should be provided to avoid overdose. Special syringes can be used to avoid dosing errors when using higher-concentration formulations.

Another delivery option is prefilled insulin pens, which offer convenience and may help to avoid certain types of medication errors. In addition, implantable programmable insulin pumps are available that can administer insulin continuously through a catheter. Some pumps have internal glucose sensors to monitor levels (refer to Figure 23-4).


Rob Byron/Shutterstock.com.

Click and Photo/Shutterstock.com.

(A) **(B)**

Figure 23-4 (A) Insulin pen: adjustable insulin dosage pen to regulate blood sugar levels. (B) Insulin pump: programmable implanted insulin pump administering continuous insulin subcutaneously to the fatty tissue layer. This pump has a glucose sensor to monitor glucose levels and adjust dosages.

An inhaled insulin product is available for clinical use under the brand name Afrezza. Since it is a rapid-acting insulin, it is meant to be used before meals to prevent the rise in blood sugar associated with food. Different doses may be delivered by picking either a 4- or 8-unit cartridge, which is loaded into an inhaler device for patient administration.

Insulin preparations differ mainly in their onset, peak, and duration of action (Table 23-4). Aspart, glulisine, and lispro insulins are *ultra-rapid acting* and have a *very short duration* of action. *Regular* insulin is *rapid acting* and has a *short duration.*

Regular insulin may be given intravenously and intramuscularly as well as subcutaneously. Aspart, glulisine, and lispro are clear and rapid acting (onset in approximately 15 min). They peak in about 1 h and last approximately 4 h. They may be given subcutaneously or intravenously. *Isophane* (NPH) is intermediate acting; glargine and detemir are long acting, and they are administered subcutaneously.

Rapid- or short-acting insulin is sometimes combined with isophane insulin in the same syringe. When two insulins are ordered at the same time, *the rapid- or short-acting insulin should be drawn into the syringe first.* Combinations of NPH and regular insulin are also available, for example, Humulin 70/30 or Novolin 70/30. This combination provides rapid onset with a duration of up to 24 h. Insulin *glargine* and insulin mixtures should not be mixed with any of the other types of insulin.

Table 23-4 Insulins

Action	Preparation	Trade Name	Onset	Peak	Duration
Rapid	aspart	Novolog	10–30 min	1–2 h	3–8 h
	glulisine	Apidra			
	lispro	Humalog			
Short	regular	Humulin R Afrezza (inhaled)	30–60 min	1–5 h	6–10 h
		Novolin R			
Intermediate	isophane (NPH)	Humulin N	1–3 h	6–12 h	18–24 h
		Novolin N			
Long	glargine	Lantus Basaglar	1–2 h	No pronounced peak	Up to 24 h (dose dependent)
Ultra-long acting	detemir	Levemir	1–2 h		
	glargine	Tresiba	1–2 h	No pronounced peak	Improved glycemic control
	degludec	Toujeo		No pronounced peak	Up to 24 h (more gradual release of insulin than Lantus)
Mixtures	NPH/reg	Humulin/Novolin 70/30, 50/50	30–60 min	1–4 h	16–24 h
	NPH/lispro	Humalog Mix 75/25, 50/50	15–30 min	1–6 h	12–24 h
	NPH/aspart	Novolog Mix 70/30	10–20 min	1–4 h	up to 24 h

Note: This is a representative list. Other insulin products are also available. Dosage varies. Because of limited use, beef- and pork-derived insulins and lente and ultralente insulins are no longer available in the United States. Before giving insulin, always check the expiration date on the vial and be sure that regular, aspart glulisine, and lispro insulins are clear and isophane insulins are cloudy. Isophane insulins are administered only subcutaneously, never IV. Rotate administration sites with each injection. Levemir, Novolin N, R, and 70/30 can be used for up to 42 days after opening when stored at room temperature. Opened vials of all other types of insulin may be stored at room temperature without loss of potency for 28 days. Stability of insulin pens and cartridges at room temperature varies depending on the product; they are never to be shared among patients, as this may result in the transmission of blood-borne pathogens.

Diabetes therapy with insulin focuses initially on controlling fasting plasma glucose with the use of a long-acting insulin analog (Lantus or Levemir). If further glycemic control is needed, a mealtime (also known as bolus or prandial) rapid- or short-acting insulin may be added to reduce postmeal hyperglycemia. Regular insulin is best given 30–60 min before a meal. The rapid-acting insulins can generally be given 15 min before or immediately after a meal. Insulin mixtures should be given within 15 min before a meal.

Rapid- or short-acting insulin is sometimes ordered as *corrective dose insulin*. This means that the blood is tested for glucose and a specific amount of insulin is administered subcutaneously based on the glucose level shown by the test. Doses are adjusted according to blood glucose response and insulin resistance (the amount of daily insulin required by patients in low-, medium-, and high-dose categories). For example, the physician might write an order to give rapid- or short-acting insulin subcutaneously with the following corrective dose scale according to the blood glucose levels:

Blood Glucose	**Dosage of Rapid- or Short-acting Insulin**		
	Low	**Medium**	**High**
>350 mg/dL	5 units	8 units	12 units and Call physician
301–350 mg/dL	4 units	7 units	10 units
251–300 mg/dL	3 units	5 units	7 units
201–250 mg/dL	2 units	3 units	4 units
151–200 mg/dL	1 unit	2 units	3 units
120–150 mg/dL	0 unit	1 unit	2 units
<120 mg/dL	No insulin		

Remember, this is only a *sample* corrective dose scale. It is now recommended that the traditional sliding scale coverage be reserved for patients who are newly diagnosed as diabetic to establish insulin requirements, started on enteral or parenteral nutrition, or started on glucocorticoids (e.g., prednisone). *Always check the physician's order carefully to determine the exact dosage of insulin, which varies with the individual.* Verification of insulin dosage with another caregiver is very important to prevent one of the most common and most dangerous of medication errors.

There are many different types of insulin available, and many have names or packages that are similar. There has been confusion between Lente and Lantus, and Humulin and Humalog. Confusion is also possible with the premixed products Humulin 70/30, Humalog Mix 75/25, Novolog Mix 70/30, and Novolin 70/30. Additionally, many brand-name insulins like Humalog and Novolog are now available in generic formulations. *Be extremely careful to give the right insulin and the right dose! If in doubt, consult the pharmacist.*

Hyperglycemia

Hyperglycemia, or elevated blood glucose, may result from:

- Undiagnosed diabetes
- Insufficient insulin dose
- Infections
- Surgical or other trauma
- Emotional stress
- Other endocrine disorders
- Medications (e.g., glucocorticoids such as prednisone)
- Pregnancy

Symptoms of hyperglycemia may include:

- Dehydration and excessive thirst
- Anorexia and unexplained weight loss in persons under 40 years old
- Polyuria (frequent urination)
- Fruity breath
- Lethargy, weakness, flu symptoms, and coma if untreated
- Vision problems
- Ketoacidosis (can be determined by testing urine for acetone)

Treatment of acute hyperglycemia includes:

IV fluids to correct electrolyte imbalance

Adding *regular* insulin to IV fluids

Interactions: Insulin action is antagonized by corticosteroids and epinephrine, necessitating increased insulin dosage. Atypical antipsychotics, protease inhibitors, thiazide diuretics, oral contraceptives, and estrogen may also increase insulin requirements. Beta-blockers (nonselective) taken with insulin pose risks of hypoglycemia or hyperglycemia and can mask the signs and symptoms (especially tachycardia) of hypoglycemia. Thiazolidinediones (Actos and Avandia) taken with insulin result in an increased risk of heart failure and edema.

Interactions of insulin with *potentiation of hypoglycemic effect* occur with:

Alcohol

Monoamine oxidase inhibitors (MAOIs)

Salicylates

Anabolic steroids

Hypoglycemia

It is estimated that 90% of all patients receiving insulin will experience a hypoglycemic event. **Hypoglycemia**, or lowered blood glucose, may result from:

Overdose of insulin and/or other antidiabetic medications

Delayed or insufficient food intake (e.g., dieting)

Excessive or unusual exercise

Change in the type of insulin, for example, from analog to human insulin

Symptoms of hypoglycemia may develop suddenly and are usually manifested at the peak of insulin action, including:

Increased perspiration, pallor, hunger, nausea, and vomiting

Irritability, confusion, or sudden unexplained bizarre moodiness or behavior change

Tremor, weakness, headache, hypothermia, or tingling of the fingers

Blurred or double vision

Tachycardia and shallow breathing

Loss of consciousness and convulsions if untreated

Hypoglycemic reactions in older adults with diabetes may mimic a CVA (cerebrovascular accident)

Treatment of hypoglycemia includes:

If conscious, administration of 4 oz orange juice, candy, honey, or syrup (especially sublingual for faster absorption). After initial treatment, provide a protein snack, for example, peanut butter, cheese, or a glass of milk. Then recheck blood glucose.

If comatose, administration of 10–30 mL of 50% dextrose solution IV or administration of 0.5–1 unit of glucagon (1 mg) SC, IM, or IV—follow with carbohydrate snack when the patient awakens to prevent secondary hypoglycemia.

Avoid giving excessive amounts of sugar or frequent overdoses of insulin, which can result in rebound hyperglycemia (Somogyi effect) from an accelerated release of glucagon. Treatment of rebound hyperglycemia involves reduction of insulin dosage with continuous monitoring of blood glucose.

Oral and Injectable Noninsulin Antidiabetic Agents

Type 2 diabetes results from insulin resistance (insulin produced but not used effectively by cells) combined with relative insulin deficiency. Type 2 diabetes is the leading cause of kidney failure, lower-limb amputations, and new cases of adult blindness. Patients may sometimes be treated with diet alone: that is, a low-calorie, low-fat diet; avoiding simple sugars and alcohol; and substituting complex carbohydrates, such as whole-grain bread and cereals, brown rice, and vegetables high in fiber.

Frequently, however, it is necessary to combine diet and oral antidiabetic agents. Oral antidiabetic agents may be administered as a single daily dose before breakfast or two divided doses daily, before morning and evening meals. These medications are not a substitute for dietary management. Weight reduction, exercise, education, and modified diet are still considered the principal therapy for the management of type 2 diabetes.

Symptoms of type 2 diabetes may include:

Excessive weight gain after age 40 years

Excessive thirst (polydipsia)

Excessive urination (polyuria)

Excessive weakness, poor circulation, and slow healing

Visual problems

Oral and injectable noninsulin antidiabetic agents are available in several pharmacological classes with differing mechanisms of action, offering different avenues for reducing glucose levels. Because they work at different sites, they are often synergistic; some may be used in combination with one another or with insulin.

Biguanides

The biguanides, for example, metformin (Glucophage), work by decreasing hepatic glucose production and enhancing insulin uptake in muscle tissue. Metformin is the preferred initial first-line monotherapy, or it can be used in combination with sulfonylureas, alpha-glucosidase inhibitors, or insulin to treat type 2 diabetes or pre-diabetes.

Side effects of biguanides may include:

❗ GI effects (diarrhea, nausea, vomiting, bloating, flatulence, metallic taste, anorexia, and weight loss), which are generally mild and resolve during treatment; can take the medication with food to minimize epigastric discomfort

Lactic acidosis (a rare but serious metabolic complication) in patients with a history of ketoacidosis, severe dehydration, cardiorespiratory insufficiency, renal dysfunction, or chronic alcohol use disorder with liver damage

Vitamin B_{12} deficiency (patients may present with peripheral neuropathy)

Cautions or contraindications for biguanides apply to:

Impaired liver and kidney function

Patients with heart failure requiring pharmacologic treatment

Administration of radiocontrast dye (could result in acute alteration of renal function; withhold metformin just prior to tests with radioactive dye and for 48 h after completion of the procedure)

Pregnancy and lactation

Children and older adults (especially those who are frail, anorexic, or underweight)

Drug interactions with biguanides include:

Increased metformin effect experienced with alcohol, cephalexin, and cimetidine

Radiopaque contrast media (refer to contraindications)

Sulfonylureas

The oral hypoglycemic drugs known as **sulfonylureas** consist of first-generation agents (e.g., chlorpropamide, tolbutamide) and second-generation agents (e.g., glipizide, glyburide). Due to their higher potency, shorter duration of action, better user tolerance, and fewer drug interactions, the second-generation agents have mostly replaced the first-generation agents. The sulfonylureas work by increasing insulin production from the pancreas and by improving peripheral insulin activity. Although patients initially respond well to this class of drugs, glycemic control begins to wane after 1 to 2 years in most patients.

Side effects of sulfonylureas may include:

❗ GI distress (may subside with dosage regulation)

Dermatological effects, including pruritus, rash, urticaria, or photosensitivity

❗ Hypoglycemia, especially in older adults—must eat consistently while on sulfonylureas

Weight gain and water retention

Cautions or contraindications for sulfonylureas apply to:

Patients in a severely weakened state or malnourished

Impaired liver and kidney function

Major surgery, severe infection, and severe trauma

Older adults (chlorpropamide and glyburide, which have a longer half-life, greater chance of hypoglycemia, and also a risk of inappropriate antidiuretic hormone secretion [water intoxication])

Interactions of sulfonylureas with *potentiation* of hypoglycemic effect can occur with:

Beta-blockers, MAOIs, or probenecid

Alcohol with facial flushing (disulfiram-like reaction)

Cimetidine, miconazole, fluconazole, quinolones, or sulfonamides

Salicylates and other nonsteroidal anti-inflammatory drugs (NSAIDs)

Interactions *with antagonistic action* (larger dose may be required) can occur with:

- Thyroid hormones
- Thiazide and nonthiazide diuretics
- Corticosteroids and phenothiazines
- Estrogens and oral contraceptives
- Calcium channel blockers
- Rifampin and isoniazid

When these agents are administered or discontinued in patients receiving sulfonylureas, the patient should be monitored closely for loss of diabetic control.

Alpha-Glucosidase Inhibitors

Alpha-glucosidase inhibitors such as acarbose (Precose) delay digestion of complex carbohydrates (e.g., starch) and subsequent absorption of glucose, resulting in a smaller rise in blood glucose concentrations following meals. Acarbose can be used as monotherapy or part of a combination regimen that includes insulin, metformin, or an oral sulfonylurea.

Side effects of alpha-glucosidase inhibitors may include:

- ❗ High rate of GI effects (flatulence, abdominal distention/pain, loose stools), which tend to diminish with time or a reduction in dose; take at the start (with the first bite) of main meals
- Elevated liver enzymes (dose-related, generally asymptomatic, and reversible)

Cautions or contraindications for alpha-glucosidase inhibitors apply to:

- Impaired liver and kidney function
- Patients with inflammatory bowel disease or intestinal obstruction
- Pregnancy and lactation
- Children

Drug interactions occur between alpha-glucosidase inhibitors and:

- Digestive enzymes (effect of acarbose reduced)
- Digoxin (reduced serum digoxin concentrations)
- Estrogens and oral contraceptives (impaired glucose tolerance)

GLP-1 Agonists (Incretin mimetics)

GLP-1 agonists act to mimic the action of a naturally-occurring hormone called GLP-1, which is released by cells in response to food. When blood sugar levels start to rise after a person eats, agents that mimic the action of GLP-1 stimulate the body to produce more insulin (the same as the naturally occurring GLP-1 and other incretins). The extra insulin helps lower blood sugar levels. Lower blood sugar levels are helpful for controlling type 2 diabetes and can also lead to weight loss.

An example of a GLP-1 agonist is exenatide (Byetta), which was one of the first approved drugs in this class. Bydureon is a long-acting form of the medication in Byetta and is given subcutaneously once weekly. Exenatide and other GLP-1 agonists are indicated as adjunctive therapy for patients with type 2 diabetes who have not achieved glycemic control and are taking metformin, a sulfonylurea, or a glitazone. Many other GLP-1 agonists are now available and are listed in Table 23-5.

At one time, GLP-1 agonists were used off-label frequently in patients with obesity to take advantage of the side effect of weight loss, even if the patient did not have a diabetes diagnosis. Today, three GLP-1 agonists are currently approved for weight loss. Tirzepatide (under the brand name Zepbound), liraglutide (Saxenda) and semaglutide (Wegovy). Tirzepatide, when used for diabetes, is available under the brand name Mounjaro. Semaglutide (Ozempic) is approved for diabetes but does not have approval for weight-loss use; however, it is still commonly used for both purposes.

Common ***side effects*** include nausea or vomiting, diarrhea, dyspepsia, gastroesophageal reflux, injection site reactions, and hypoglycemia (when given in combination with sulfonylureas). It is not recommended for use in patients with severe renal disease or a history of pancreatitis.

DPP-4 Inhibitors

Sitagliptin (Januvia), saxagliptin (Onglyza), and linagliptin (Tradjenta), given *orally* once daily, are indicated for use as monotherapy in patients with type 2 diabetes or in combination with other agents when adequate glycemic control has not been achieved. They may be preferred agents in older adults.

Common ***side effects*** include abdominal pain, diarrhea, nausea, vomiting, upper respiratory tract infection, and nasopharyngitis. Use these agents with caution (if at all) in patients with a history of pancreatitis. Dosage adjustments are required for renal disease (except for linagliptin).

Meglitinides

Nateglinide (Starlix) and repaglinide (Prandin) stimulate the beta cells of the pancreas to produce insulin. They can be used as monotherapy or in combination with metformin. Meglitinides have a rapid onset and short duration of action, and are to be taken before each meal.

Side effects of meglitinides may include:

- ❗ GI effects (nausea or vomiting, diarrhea, constipation, dyspepsia, and abdominal cramps)
- ❗ Hypoglycemia; initial weight gain
- ❗ Upper respiratory infection (URI), sinusitis, arthralgia, and headache

Cautions or contraindications for meglitinides apply to:

Diabetic ketoacidosis

Impaired liver function

Pregnancy and lactation

Children

Drug interactions with meglitinides include (also refer to the listing under sulfonylureas):

Administer before meals to maximize absorption

Gemfibrozil (Lopid) may enhance or prolong effects

Thiazolidinediones

Pioglitazone (Actos) and rosiglitazone (Avandia) lower blood glucose by decreasing insulin resistance and improving sensitivity to insulin in muscle, liver, and adipose tissue. They can be used as monotherapy or concomitantly with other agents.

Product labeling for both pioglitazone and rosiglitazone includes black box warnings regarding the potential for these agents to cause or exacerbate congestive heart failure in some patients, and both are contraindicated with class III and class IV heart failure. In addition, a black box warning for the potential increase in the risk of myocardial ischemia has been added to rosiglitazone's label, although the warning also states that the data concerning the increased risk of myocardial ischemia are inconclusive. Because of these precautions, only patients who are already established on this medication are normally given prescriptions for it. Additionally, physicians who wish to prescribe this medication must be registered with the Avandia-Rosiglitazone Medicine Access Program.

Side effects of thiazolidinediones may include:

❗ Weight gain, fluid retention, and edema (report weight gain over 6.6 lb, sudden onset of edema, or shortness of breathc)

❗ URI, sinusitis, pharyngitis, and headache

❗ Myalgia; atypical bone fractures (upper arm, hand, and foot)

Anemia

❗ Hypoglycemia (in combination with insulin or oral hypoglycemics)

Cautions or contraindications for thiazolidinediones apply to:

Impaired liver function

Heart failure (causes edema); pulmonary edema

May cause resumption of ovulation in premenopausal patients, increasing the risk for pregnancy

Pregnancy and lactation

Children

Drug interactions occur between thiazolidinediones and:

Insulins (increase the probability of weight gain, fluid retention, and heart failure

Pioglitazone with oral contraceptives (reduced effectiveness of the contraceptive)

Rosiglitazone with nitrates (increased risk of myocardial ischemia)

"Azole" antifungals (potentiation of hypoglycemic effect)

SGLT2 Inhibitor Therapy

Sodium-glucose co-transporter 2 inhibitors are the newest class of antidiabetic medications. Like other oral and injectable noninsulin medications, they are only indicated for use in patients with type 2 diabetes. They can be used as monotherapy or in combination with oral medications. They work by decreasing the reabsorption of glucose in the kidneys, essentially lowering glucose available to the body via excretion. Current drugs in this class include canagliflozin (Invokana), empagliflozin (Jardiance), ertugliflozin (Steglatro), dapagliflozin (Farxiga), and bexaglifloxin (Brenzavvy). The most common ***side effects*** with these medications are vaginal yeast infections and urinary tract infections, along with increased desire to urinate.

Refer to Table 23-5 for a summary of the oral hypoglycemics.

Table 23-5 Oral and InjecTable Noninsulin Antidiabetic Agents

Generic Name	Trade Name	Usual Dosage
First-Generation Sulfonylureas		
chlorpropamide	Diabinese	PO 100–500 mg per day with meal (do not use for older adults)
tolbutamide	Orinase	PO 250–3,000 mg per day or divided
Second-Generation Sulfonylureas		
glimepiride	Amaryl	PO 1–8 mg per day with meal
glipizide	Glucotrol	PO 2.5–40 mg per day ac or divided
	Glucotrol XL	PO 5–20 mg per day with meal
glyburide	Diabeta	PO 1.25–20 mg per day or divided with meal
	Glynase (micronized)	PO 1.5–12 mg per day with meal
Alpha-Glucosidase Inhibitors		
acarbose	Precose	PO 25–100 mg tid, with first bite of meal
miglitol	Glyset	PO 25–100 mg tid, with first bite of meal
Biguanides		
metformin	Glucophage	PO 500–2,550 mg per day divided with meals
	Glucophage XR	PO 500–2,000 mg per day with p.m. meal or divided
GLP-1 Agonists (Incretin mimetics)		
exenatide	Byetta	SQ 5–10 mcg bid ac (a.m. & p.m. meal)
	Bydureon	SQ 2 mg weekly (any time of day)
dulaglutide	Trulicity	SQ 0.75–1.5 mg weekly
liraglutide	Victoza	SQ 0.6–1.8 mg daily for diabetes
	Saxenda	SQ 0.6–1.8 mg daily for weight loss
tirzepatide	Mounjaro	SQ 2.5–5 mg weekly for diabetes
	Zepbound	SQ 2.5–15 mg weekly for weight loss
semaglutide	Ozempic	SQ 0.25–2 mg weekly for diabetes
	Wegovy	SQ 0.25–1.7 mg weekly for weight loss

(*Continued*)

Table 23-5 Oral and InjecTable Noninsulin Antidiabetic Agents (*Continued*)

Generic Name	Trade Name	Usual Dosage
DPP-4 inhibitors ("gliptins")		
alogliptan	Nesina	PO 25 mg daily
linagliptin	Tradjenta	PO 5 mg daily
sitagliptin	Januvia	PO 50–100 mg daily
saxagliptin	Onglyza	PO 2.5–5 mg daily
Meglitinides		
nateglinide	Starlix	PO 60–120 mg tid ac
repaglinide	Prandin	PO 0.5–4 mg bid two to four times per day ac
Thiazolidinediones		
pioglitazone	Actos	PO 15–45 mg per day
rosiglitazone	Avandia	PO 4–8 mg per day or bid divided (restricted access/distribution)
SGLT2 Inhibitors		
canagliflozin	Invokana	PO 100–300 mg daily in the morning before first meal of day
empagliflozin	Jardiance	PO 10–25 mg daily in the morning with or without food
ertugliflozin	Steglatro	PO 5–15 mg in the morning before first meal of day
dapagliflozin	Farxiga	PO 5–10 mg daily in the morning with or without food
bexaglifloxin	Brenzavvy	PO 20 mg daily in the morning with or without food
Combinations		
glyburide/metformin	Glucovance	PO 1.25/250–20/2,000 mg per day or bid with meals
rosiglitazone/metformin	Avandamet	PO 2/500–8/2,000 mg per day with meals or divided (restricted access/distribution)
sitagliptin/metformin	Janumet Janumet XR	PO 50/500–50/1,000 mg bid with meals PO 50/1,000–100/2,000 mg daily
Saxagliptin/metformin	Kombiglyze XR	PO 5/500 mg daily
Canagliflozin/metformin	Invokamet Invokamet XR	PO 50/500–150/1,000 mg bid PO 100/1,000–300/2,000 mg daily
Empagliflozin/metformin	Synjardy Synjardy XR	PO 5/500–12.5/2,000 mg bid PO 10/1,000–25/1,000 mg daily

Notes: In older adults, start with the lowest dose possible and titrate upward to achieve desired glycemic control.

This is a representative list, other products may be available.

Patient Education

Patients with both type 1 and type 2 diabetes should be instructed regarding:

Prevention of hypoglycemia—the importance of control with proper drug and diet therapy and *never* skipping meals; do not consume alcohol on an empty stomach

Early symptoms and treatment of hypoglycemia—carrying a ready source of carbohydrate (e.g., glucose tablets, lump sugar, or candy); orange juice, 4 oz, is also appropriate

Properly balanced diet (i.e., restricted calories); avoidance of simple sugars, alcohol, and foods high on the glycemic index (e.g., white bread, white potatoes, and white rice)

Substitute foods low on the glycemic index—complex carbohydrates, such as whole-grain breads and cereal, and brown rice; reduce fats, increase fiber, and be sure to have adequate fluid intake

Regular exercise and maintenance of proper body weight; weight reduction if obese

Importance of reporting to a physician *immediately* if nausea, vomiting, diarrhea, or infections occur (IV fluids may be required to prevent dehydration and acidosis)

Good foot care to reduce the chance of infections

Carrying identification card and wearing identification tag

Drugs with similar brand or generic names: Actos/Actonel, glipizide/glyburide, insulin name pairs mentioned earlier

Taking the medication (oral or insulin) at approximately the same time each day and in proper relation to meals

Proper use of monitoring devices; check blood glucose as directed by the physician, especially with hypoglycemia or stress

For patients with type 1 diabetes and patients with type 2 diabetes who require insulin, the aforementioned instructions are important, as well as these additional rules:

Rotate injection sites (Figure 23-5). Insulin is absorbed more rapidly in the arm or thigh, especially with exercise. Inject insulin into the abdomen if possible for the most consistent absorption.

Maintain aseptic technique with injections.

Have someone check the amount of insulin in the syringe or pen before injection, especially with older adults or those with low vision (retinal problems are common in diabetics).

Check all insulin for the expiration date.

Check regular insulin for clearness; do *not* give if cloudy or discolored.

Rotate isophane insulin vials to mix contents; do *not* give if solution is clear or clumped in appearance after rotation; do not shake the vial; rotate gently between hands (Figure 23-6).

If regular insulin is to be mixed with NPH, draw regular insulin into the first.

Unopened vials of insulin should be stored at 2°C–8°C and should not be subjected to freezing. The vial or pen in use may be stored at room temperature for a limited amount of time (depending on the product) without loss of potency.

Avoid exposure of insulin to extremes in temperature or direct sunlight. Do not put vial in glove compartment, trunk, or suitcase.

Regular insulin is sometimes administered as correction for elevated blood glucose readings as ordered by a physician.

Properly dispose of injectable products.

Notify the physician of illness, increased stress, or trauma. *More* insulin may be required under these circumstances.

Notify the physician if the patient increases exercise significantly or if taking less than the usual amount of food. *Less* insulin may be required under these circumstances.

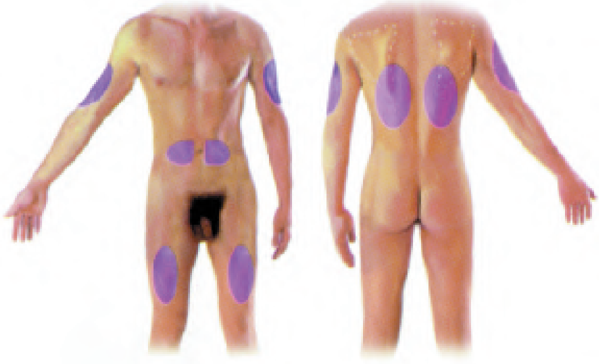


Figure 23-5 Common sites for insulin injection. Sites should be rotated and the site recorded each time on the medication record.

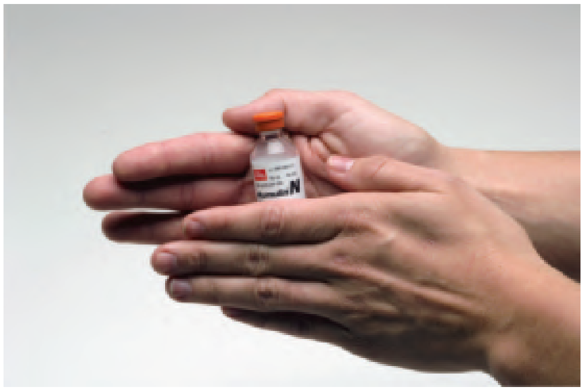


Figure 23-6 Rotate isophane and zinc insulin vials gently to mix contents. Do not shake.

Case Study A

Endocrine System Drugs

After weeding in their garden, a patient experiences a severe allergic reaction to poison ivy. They present with a rash on their face, arms, and legs.

1. The physician prescribes a corticosteroid. How will this category of medication be most beneficial?
   a. As an antipruritic
   b. As an antineoplastic
   c. As an antidiabetic
   d. As an anti-inflammatory
2. The physician explains that side effects of the corticosteroid may include:
   a. Hypotension
   b. Hypoglycemia
   c. Increased susceptibility to infection
   d. Flushing of the hands and face
3. The physician reviews the patient's medication history. They know this is essential because of possible interactions with corticosteroids. Which drug may cause an interaction resulting in reduced effectiveness of the corticosteroid?
   a. Estrogen
   b. Salicylates
   c. Diuretics
   d. Phenytoin
4. When the patient picks up the corticosteroid medication at the pharmacy, they read the label on the side of the bottle containing instructions on when to take the medication. Which of the following is most likely to be on this label?
   a. Take 1 h before meals.
   b. Avoid taking with milk.
   c. Take 1 h after meals.
   d. Take 2 h after meals.
5. The patient will be taking the medication for a prescribed amount of time. What will be the best method to discontinue the corticosteroid?
   a. Slowly taper the dosage
   b. Stop the medication abruptly
   c. Reduce the dose in alternating weeks
   d. Administer an IV bolus and then discontinue the medication

Case Study B

Antidiabetic Agents

A patient has been diagnosed with new onset of type 2 diabetes. The physician orders a low-fat, low-calorie diet. In addition to dietary changes, the physician would like to start the patient on metformin and another oral hypoglycemic drug.

1 The physician starts the patient on glyburide, a sulfonylurea medication. The physician explains to the patient that sulfonylureas work by:
- a. Blocking glucose uptake into the cell
- b. Increasing insulin production from the pancreas
- c. Decreasing glucagon secretion
- d. Promoting urinary excretion of excess glucose

2. The physician explains to the patient that one of the side effects of a sulfonylurea medication is:
- a. Insomnia
- b. Orthostatic hypotension
- c. Excessive urination
- d. Fatigue

3. Prior to prescribing the medication, the physician reviews the patient's medical history. This is because sulfonylureas must be used with extreme caution in individuals who:
- a. Are obese
- b. Are asthmatic
- c. Have impaired kidney and liver function
- d. Have peripheral vascular disease

4. The physician cautions the patient to contact the office prior to taking any other medication because of possible interactions. Which drug can potentiate the hypoglycemic effect of a sulfonylurea?
- a. Quinolones
- b. Penicillins
- c. Antacids
- d. Rifampin

5. What drug causes an interaction with sulfonylureas, resulting in an antagonistic action in which a larger dose may be required?
- a. MAOIs
- b. Testosterone
- c. Corticosteroids
- d. Narcotic analgesics

Chapter Review Quiz

Match the medication in the first column with the appropriate classification in the second column. Classifications may be used more than once.

Medication

1. ________ Glucophage

2. ________ prednisone

3. ________ Humulin R

4. ________ Synthroid

5. ________ Avandia

6. ________ Tapazole

7. ________ Isophane

8. ________ Prandin

9. ________ Lantus

10. ________ Humalog

Classification

a. Thyroid agent

b. Antithyroid

c. Oral antidiabetic agent

d. Corticosteroid

e. Insulin—rapid acting

f. Insulin—short acting

g. Insulin—intermediate acting

h. Insulin—long acting

Choose the correct answer

11. The biguanide that decreases hepatic glucose production and enhances insulin uptake is which of the following?

a. Glucophage

b. Starlix

c. Synthroid

d. Cortrosyn

12. NTIs are characterized by which of the following?

a. Very high doses are needed to show effects.

b. They have a small range at which they are safe and effective.

c. They are administered with a narrow-gauged needle.

d. They do not require laboratory monitoring upon initialization.

13. A patient who is on a thyroid medication should be monitored for which potential side effect?

a. Hyperglycemia

b. Hypotension

c. Muscle twitching

d. Shortness of breath

14. Thyroid medication should be taken:

a. At bedtime with a sip of water

b. On an empty stomach 30–60 min prior to breakfast

c. 30–60 min after breakfast

d. With breakfast

15. Insulin is administered parenterally because:

a. It is easier to monitor dosage
b. It is destroyed in the GI tract
c. Insulin pills are difficult to swallow
d. Parenteral dosing is tolerated better

16. To prevent a medication error, an insulin dose in a syringe:

a. Should be color-coded for specific doses
b. Should be drawn up with the nondominant hand for a better visualization of the dose
c. Should be verified only by a pharmacist
d. Should be verified by another clinician

17. What best describes the onset and duration of action of regular insulin?

a. Delayed onset and short duration
b. Extended onset and long duration
c. Rapid onset and short duration
d. Ultra-rapid onset and very short duration

18. The peak of rapid-acting insulins falls under which time frame postinjection?

a. 1–2 h
b. 1–5 h
c. 6–12 h
d. 12–24 h

19. What is one of the most likely symptoms of hyperglycemia?

a. Weight gain
b. Excitability
c. Excessive thirst
d. Urinary retention

20. Which of the following may potentiate the hypoglycemic effect of insulin?

a. NSAIDs
b. Corticosteroids
c. Antidepressants
d. Alcohol

21. Which preparation of insulin is used to correct elevated blood glucose?

a. Lispro
b. Regular
c. isophane (NPH)
d. Glargine

22. Illness, increased stress, or trauma may have what effect on a prescribed dose of insulin?

a. Less insulin may be required.
b. The dose will need to be divided.
c. More insulin may be required.
d. No change in dosage will be required.

23. Which of the following is the main type of side effect observed with SGLT2 inhibitors?

a. Urinary
c. Dermal
b. Respiratory
d. Gastric

24. In what scenario would steroid tapering be most important when discontinuing corticosteroid therapy?

a. When oral therapy exceeds 14 consecutive days at a dose of 20 mg of prednisone (or equivalent) per day or more
b. When topical therapy is used daily for 30 days or more
c. When inhaled therapy is used at a dose of 50 mcg for 14 days or more
d. When a single oral dose of 50 mg is administered

25. Thyroid replacement therapy, like levothyroxine, should be taken when?

a. In the evening on an empty stomach before bedtime with other night-time medications.
b. In the morning with the first meal of the day.
c. Anytime, as long as it is taken at the same time each day with food.
d. First thing in the morning on an empty stomach.

Chapter 24

Reproductive System Drugs

Key Terms and Concepts

Androgens
Contraceptives
Erectile dysfunction (ED)
Estrogen and progestin therapy (EPT)
Estrogens
Estrogen therapy (ET)
Follicle-stimulating hormone (FSH)
Hormone therapies (HTs)
Luteinizing hormone (LH)
Luteotropic hormone (LTH)
Oxytocin
Progesterone
Progestins
Testosterone
Tocolysis

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify the uses, side effects, and precautions for the androgens.
2. List the uses, side effects, and precautions or contraindications for the estrogens and progestins.
3. Describe the various types of contraceptives and how they are similar and different.
4. Describe the use of oxytocics and the precautions to be observed.
5. Explain the uses of terbutaline, prostaglandins, and magnesium sulfate.
6. Explain drug therapy for erectile dysfunction.
7. Describe the other gonadotropic drugs.

Hormones that regulate the functions of the reproductive systems include *endogenous* chemical substances, which originate within different areas of the body. For simplification, we will divide the reproductive hormones into four main categories: gonadotropic, androgens, estrogens, and progestins.

The pituitary gland is located at the base of the brain. The anterior lobe secretes four hormones. This chapter discusses the gonadotropic hormones, which are secreted by the anterior and posterior pituitary lobes.

Gonadotropics

The gonadotropic hormones include (1) **follicle-stimulating hormone (FSH)**, which stimulates the development of ovarian follicles in the female and sperm production in the testes of the male; (2) **luteinizing hormone (LH)**, which works in conjunction with FSH to induce secretion of estrogen, ovulation, and development of the corpus luteum; and (3) **luteotropic hormone (LTH)**, which stimulates the secretion of progesterone by the corpus luteum and secretion of milk by the mammary gland, hence the term *lactogenic hormone*.

Androgens

Androgens, the male sex hormones, are secreted mainly in the interstitial tissue of the testes in the male and secondarily in the adrenal glands of both sexes. Androgens, which stimulate the development of male characteristics (masculinization), include **testosterone** and androsterone.

Inadequate production of androgens in the male may be because of pituitary malfunction or due to atrophy of, injury to, or removal of the testicles (castration), resulting in eunuchism or eunuchoidism. Eunuchoid characteristics include delayed development of sex organs, absence of beard and body hair, high-pitched voice, and lack of muscular development. Hypogonadism may also result in impotence or oligospermia (deficient sperm production).

Testosterone is absorbed from the gastrointestinal (GI) tract, but because of extensive metabolism by liver enzymes, oral bioavailability is poor. Replacement therapy is currently available in buccal, parenteral, and transdermal formulations. Synthetic androgens such as danazol and methyltestosterone are available for oral use but are used more often for conditions other than replacement therapy (refer to the following list) and have an increased potential for liver abnormalities.

Uses of androgens include:

Replacement in cases of diminished testicular hormone with testosterone (e.g., impotence, oligospermia, or andropause [“male menopause”])

Congenital hypogonadism (e.g., cryptorchidism or undescended testicles) or delayed puberty in the male

Acquired hypogonadism (e.g., orchitis, trauma, tumor, radiation, surgery of the testicles, or drug-induced)

Palliative treatment of females with advanced metastatic carcinoma of the breast, for example, methyltestosterone (acting as an antiestrogen)

Treatment of endometriosis and fibrocystic breast disease, for example, danazol, which is antiestrogenic and weakly androgenic

Treatment of cachexia with oxandrolone, an anabolic steroid with much greater anabolic effects than androgenic effects, thus promoting weight gain in patients with burns, trauma, AIDS, or chronic obstructive pulmonary disease (COPD)

Side effects of androgens can include:

❗ Edema and hypertension (diuretics may be indicated)

❗ Acne, increased oiliness of the skin and hair, or alopecia (male pattern baldness)

Oligospermia (deficient sperm production resulting in sterility)

Increased or decreased sexual stimulation or libido and impotence

Gynecomastia in males (enlarged breast tissue)

Hirsutism (excessive or unusual growth of hair), deepening of voice, and amenorrhea or other menstrual irregularities in females

❗ Jaundice and hepatitis

Nausea and vomiting

❗ Premature closure of bone ends in adolescents, with stunting of growth

❗ Anxiety, depression, and headache

Increased low-density lipoproteins (LDLs), decreased high-density lipoproteins (HDLs), and insulin resistance

Cautions or contraindications for androgens apply to:

Cardiac, renal, and liver dysfunction (edema is common)

Males suspected of having carcinoma of the prostate or breast (stimulates growth of cancerous tissue)

Older adult males (may increase the risk of or worsen prostatic hypertrophy and carcinoma or sexual overstimulation)

Prepubertal males who have not reached their full growth potential (may stunt growth by premature closure of bone ends)

Diabetes, obesity, or dyslipidemia (abnormal lipid profile)

Interactions of androgens may occur with:

Oral anticoagulants (potentiation may cause bleeding)

Decreased blood glucose and decreased insulin requirements in those with diabetics

Antiandrogens (dutasteride and finasteride)

Dangers of illegal use of anabolic steroids: Health care personnel have a responsibility to caution athletes, especially adolescents, regarding the hazards of taking illegal synthetic testosterone products to build muscle power, or physique. Besides the *potentially serious adverse side effects* just mentioned, another risk is *the development of psychosis* with delusions, paranoia, depression, mania, and aggression with violence.

All noncombination products in this class are classified as controlled substances (C-III) by the Drug Enforcement Agency (DEA) because of their abuse potential.

Refer to Table 24-1 for a summary of the androgen agents.

Table 24-1 Androgen Agents

Generic Name	Trade Name	Dosage	Uses/Comments
danazol	Danocrine	PO 100–400 mg bid	Endometriosis, fibrocystic breast disease
methyltestosterone	Android, Testred	PO, dose varies	Advanced breast cancer; replacement therapy

(*Continued*)

Table 24-1 Androgen Agents (*Continued*)

Generic Name	Trade Name	Dosage	Uses/Comments
methyltestosterone with estrogen	Covaryx, Covaryx H.S.	PO, dose varies (given cyclically)	Menopausal symptoms if estrogen alone is insufficient
oxandrolone	Oxandrin	PO 2.5–20 mg per day in divided doses	Treatment of cachexia associated with burns, trauma, AIDS, and COPD
testosterone	Depo-Testosterone Striant Androderm AndroGel Axiron	Deep IM, pellet implant, buccal; dose varies Transdermal patch Transdermal gel Transdermal solution (apply to axilla)	Hypogonadism, advanced breast cancer, replacement therapy

Patient Education

Patients on androgen therapy should be instructed regarding:

- Taking only prescribed drugs according to directions
- Skin irritation possible with transdermal formulations
- Reporting side effects, especially edema, jaundice, nausea, or vomiting
- Reporting sexual effects for males, such as decreased ejaculatory volume and excessive sexual stimulation, especially in geriatric patients beyond cardiovascular capacity
- Sexual effects for females to expect (e.g., hirsutism and voice deepening)
- Possibility of stunted growth when administered to adolescent boys before puberty
- Need for adults using testosterone gels to avoid secondary exposure of children and partners by: 1) targeting a discreet application site such as the front and inner thighs or underarms (depending on the product used), 2) washing their hands with soap and warm water after every application, 3) covering the application site with clothing once the gel has dried, and 4) Possibility that testosterone levels may require monitoring (via blood draw) during treatment.

Erectile Dysfunction Medications

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory performance. The incidence of ED increases with age, with an increased risk in those with diabetes, cancer, stroke, and cardiovascular disease. The principal mediator in attaining and maintaining an erection is nitric oxide, which ultimately causes smooth muscle relaxation in the corpus cavernosum of the penis, allowing the inflow of blood. It should be noted that ED can be also caused by psychological factors. Although traditional ED medications discussed here may be partially useful, other classes of medication such as selective serotonin reuptake inhibitors (SSRIs) can also be used to help relieve symptoms of performance anxiety that cause ED.

Phosphodiesterase (PDE) Inhibitors

Phosphodiesterase (PDE) inhibitors are a class of drugs given orally for the treatment of ED, also referred to as impotence. Their introduction represented a significant advancement, as other therapies required direct injection into the penis (Caverject) or insertion of a urethral suppository (Muse). The PDE inhibitors block PDE type 5, found in the corpus cavernosum, which is thought to impair the production of nitric oxide.

Sildenafil (Viagra) was the first PDE inhibitor approved to treat ED, followed by vardenafil (Levitra), tadalafil (Cialis), and avanafil (Stendra). These medications require sexual arousal for success. PDE is also found in various organs and tissues such as the prostate, pulmonary arteries, other blood vessels, retina, heart, liver, and brain. Sildenafil (as Revatio) and tadalafil (as Adcirca) are also approved to treat pulmonary hypertension; tadalafil (as Cialis) is also approved for the treatment of signs and symptoms of benign prostatic hyperplasia (BPH).

Side effects of PDE inhibitors can include:

❗ Headache, flushing, vision abnormalities, and dizziness

❗ Hearing loss and tinnitus

Dyspepsia, nasal congestion, rhinitis, diarrhea, rash, and back pain

❗ Cardiovascular events (fewer than 2% of patients), including angina, syncope, tachycardia, palpitation, and hypotension

Cautions or contraindications for PDE inhibitors apply to:

Nitrates or alpha-blockers (e.g., Flomax, Cardura) (potentiates the hypotensive effects if used concurrently)

Older adults and patients with preexisting cardiovascular risk factors

Hepatic or renal function impairment

In the event of an erection persisting more than 4 h, advise the patient to seek medical assistance immediately (tissue damage and permanent loss of potency may result)

Interactions occur between PDE inhibitors and:

Nitrates, antiarrhythmics, antiretroviral protease inhibitors, macrolides, quinolones, and some antifungals (potentiate/prolong hypotensive effect)

Grapefruit juice (use with caution; may potentiate hypotensive effect)

Refer to Table 24-2 for a summary of the erectile dysfunction (ED) agents.

Table 24-2 Erectile Dysfunction (ED) Agents

Generic Name	Trade Name	Starting Dose	Uses/Comments
sildenafil	Viagra	25–100 mg PO 1 h before sexual activity (max freq once daily)	Onset of action is 15–60 min; duration is up to 4 h
	Revatio	PO 20 mg tid IV 10 mg tid	For pulmonary hypertension
tadalafil	Cialis	5–20 mg PO 1–12 h before sexual activity (max freq once daily	Onset of action is 15–45 min; duration is up to 36 h
		2.5 mg PO daily	Without regard to timing of sexual activity
		5 mg PO daily	For ED and BPH or BPH alone

(*Continued*)

Table 24-2 Erectile Dysfunction (ED) Agents (*Continued*)

Generic Name	Trade Name	Starting Dose	Uses/Comments
	Adcirca	40 mg PO daily	For pulmonary hypertension
vardenafil	Levitra	10 mg PO 1 h before sexual activity (max freq once daily)	Onset of action is 25 min; duration is up to 4 h
avanafil	Stendra	50–200 mg 30 min before sexual activity (max freq once daily)	Onset of action is 30–45 min; duration is up to 6 h

Note: ED agents do not affect the libido and have no effects in the absence of sexual stimulation.

Estrogens

Estrogens, the female sex hormones, are produced mainly by the ovaries and secondarily by the adrenal glands. Estrogens are responsible for the development of female secondary sexual characteristics, including breast enlargement, and during the menstrual cycle they act on the female genitalia to produce an environment suitable for fertilization, implantation, and nutrition of the early embryo. Estrogens also affect the secretion of the hormones FSH and LH from the anterior pituitary gland in a complex way. This results in the inhibition of lactation and ovulation; the latter process is utilized in contraceptive therapy.

Menopause is a typical, natural life event that occurs in females as part of the aging process over a period of years, but it can be artificially induced by the surgical removal of the uterus and ovaries, chemotherapy, or other medical treatments. In menopause, levels of estrogen and progesterone are reduced, leading to the development of vasomotor symptoms (e.g., hot flashes and night sweats) and atrophic vaginitis (thinning, dryness, and inflammation of the vaginal walls; refer to Figure 24-1). Historically, estrogen replacement therapy was routinely used for relieving menopausal symptoms. Estrogen (in combination with progesterone for those with an intact uterus) is used in the management of severe menopausal symptoms.

Estrogen therapy (ET), that is, estrogen alone, has been associated with an *increased risk of endometrial carcinoma* in those with an intact uterus. When progestin is combined with estrogen (*combined hormone or* **estrogen and progestin therapy [EPT]**), the risk of endometrial cancer is substantially reduced.

In 2002, the results of the Women's Health Initiative (WHI) study were released. The main thrust of the WHI study was to determine the exact degree to which **hormone therapies (HTs)** presumably protected the heart and to investigate the degree to which some of the known and potential risks of HTs, such as breast cancer and blood clots, canceled out any benefits. The WHI also explored whether HTs prevented fractures; colon cancer; and dementia, including Alzheimer's disease.

The authors of the WHI study announced not only that the risks of *combined HT* outweighed its benefits when used to prevent certain diseases, but also that the combined HT could actually *increase the risk* of certain conditions it was previously believed to prevent, such as heart attack. These findings and further research led to the establishment of the North American Menopause Society's (NAMS) new position statement on hormone therapy, which was originally published in 2012

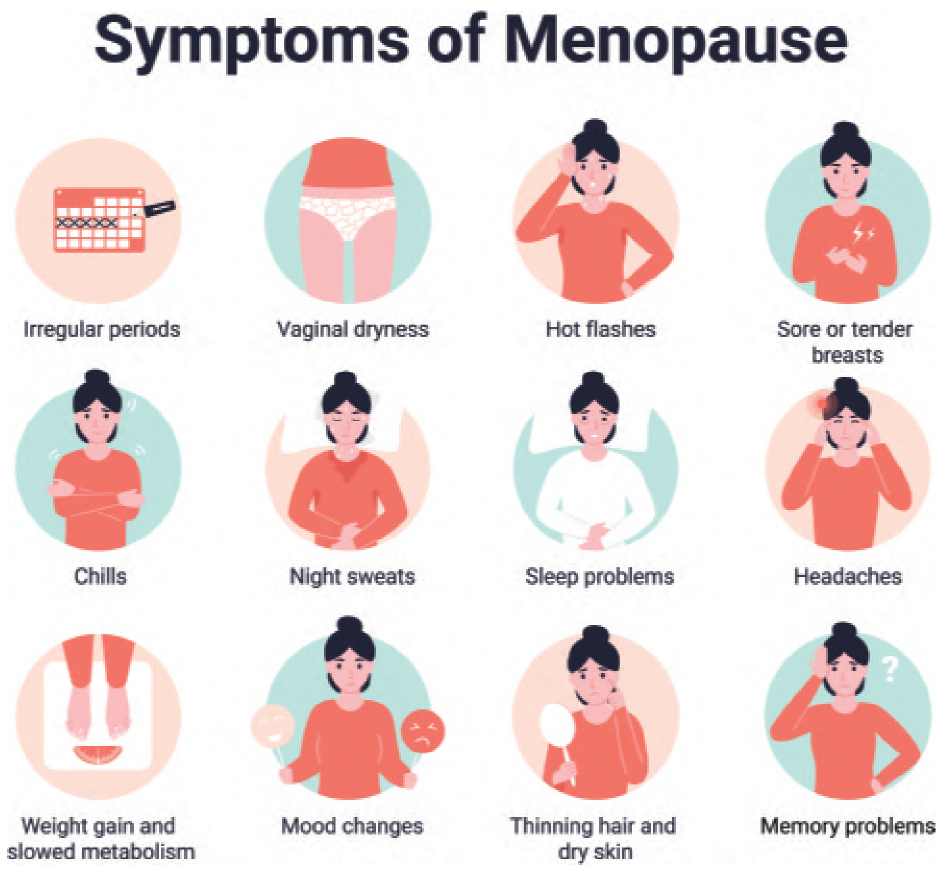

Symptoms of Menopause
Irregular periods
Vaginal dryness
Hot flashes
Sore or tender breasts
Chills
Night sweats
Sleep problems
Headaches
Weight gain and slowed metabolism
Mood changes
Thinning hair and dry skin
Memory problems

Figure 24-1 Menopause can present with various symptoms throughout the body and can change as menopause progresses.

iStock.com/Natty Blissful

and most recently updated in 2023. This represents the most recent guidelines on HT use:

- Hormone therapy remains the most effective treatment for vasomotor symptoms, including hot flashes and night sweats that can interrupt sleep and impair quality of life, and should be considered for patients in menopause and within 10 years of their final menstrual periods.
- For patients who are not good candidates for hormone therapy because of contraindications (e.g., estrogen-dependent cancers such as breast cancer, blood clots, heart disease, stroke, or personal preference), taking HT may not be recommended. It is important for health care professionals to be well informed about nonhormone treatment options for reducing vasomotor symptoms that are supported by the evidence.
- How long you should take HT is different for EPT and ET. For EPT, the time is limited by the increased risk of breast cancer that occurs with more than 3 to 5 years of use. For ET, no sign of an increased risk of breast cancer was documented during an average of 7 years of treatment, a finding that allows more choice in how long you decide to use ET.
- Most healthy females below age 60 years will have no increase in the risk of heart disease with HT. The risks of stroke and blood clots in the lungs are increased, but in these younger age groups the risks are less than 1 in every 1,000 females per year taking HT.

- ET delivered through the skin (by patch, cream, gel, or spray) and low-dose oral estrogen may have lower risks of blood clots and stroke than standard doses of oral estrogen, but all the evidence is not yet available. Research will continue to bring valuable information to help patients with their decisions about HT.

For more information about menopause, visit the NAMS website: www.menopause.org.

Uses of estrogen therapy include:

Contraceptives (combined with progestin; these combination products are also used to treat menstrual irregularities and dysmenorrhea [painful menstruation])

Menopausal vasomotor symptom relief

Female hypogonadism owing to ovarian pathology or oophorectomy (ovary removal)

Postmenopausal prevention of osteoporosis (secondary to estrogen deficiency) *only* if unable to take other agents and if benefits outweigh the risks

Atrophic vaginitis from decreased secretions (low-dose vaginal cream biweekly)

Postcoital use after unprotected sexual intercourse (within 72 h) of a single large dose to prevent, not terminate, pregnancy

Palliative treatment for males with advanced, inoperable prostate cancer

Side effects of estrogen therapy, especially with high doses, can include:

❗ Increased risk of thromboembolic disorders, hypertension, myocardial infarction, and stroke

Skin discolorations (acne may decrease or occasionally increase)

Fluid retention and edema

Increased serum triglyceride levels

Folic acid deficiency (may require folic acid supplements)

Liver function abnormalities, including jaundice, anorexia, and pruritus

Breakthrough or irregular vaginal bleeding

Increased risk of cervical erosion and *Candida* vaginitis

❗ Headache, especially migraine, and depression

Visual disturbances

Breast tenderness, enlargement, and secretion

❗ Increased risk of gallbladder disease

❗ Cancer of the uterus with estrogen alone; therefore, progesterone is recommended with estrogen (refer to the WHI study and NAMS recommendations at the beginning of this section)

Cautions or contraindications exist because the use of estrogens, especially in large doses, may be associated with the increased risk of several serious conditions. Before the estrogen therapy is begun, a complete history and physical examination are essential, and yearly physicals, including Pap test and mammogram, during therapy are important. Estrogens are contraindicated for anyone with a history of the following conditions, and estrogen therapy should be *discontinued with the signs of these conditions*:

Hypertension, thromboembolic disorders (deep vein thrombosis [DVT], pulmonary embolism [PE]), stroke, and myocardial infarction

Liver dysfunction

Breast cancer (except for palliative treatment)

Undiagnosed vaginal bleeding

Visual disturbances, severe headaches, and migraine

Shortness of breath and chest or calf pain

Pregnancy

Other cautions for estrogens include the following:

Prolonged, continued use of high-dose estrogens in patients who are postmenopausal, which has shown an increased risk of endometrial cancer in some studies; therefore, cyclic administration at the *lowest* possible dose is recommended with progesterone; regular physical examinations, including a Pap test every year, are also recommended

Pregnancy, in which estrogens can cause serious fetal toxicity, congenital anomalies, and vaginal or cervical cancer for the offspring in later life; estrogens should *never* be used to treat threatened abortions or if there is any possibility of pregnancy; a pregnancy test should be done before initiating therapy

Lactation

Diabetics and heavy smokers

Interactions of estrogen include the following:

Rifampin and isoniazid decrease estrogenic activity, and therefore other forms of contraception should be used with patients receiving rifampin or isoniazid.

Corticosteroid effects are potentiated by estrogen.

Laboratory test interference includes endocrine function tests, decreased glucose tolerance, and thyroid function tests.

Oral anticoagulant, anticonvulsant, thyroid hormone, and hypoglycemic actions may be decreased with estrogen.

Sunscreens with estradiol topical emulsion increase absorption.

Progestins

Progesterone is a hormone secreted by the corpus luteum and adrenal glands. It is responsible for changes in the uterine endometrium in the second half of the menstrual cycle in preparation for implantation of the fertilized ovum, development of the placenta after implantation, and development of mammary glands. Synthetic drugs that exert progesterone-like activity are called **progestins**.

Uses of synthetic progestins include:

Treatment of amenorrhea and abnormal uterine bleeding caused by hormonal imbalance

Contraception, either combined with estrogen or used alone

Postmenopausal—sometimes combined with estrogen in replacement cyclical therapy (note the risks)

Adjunctive and palliative therapy for advanced and metastatic endometrial or breast cancer (Megace—is also used for the anorexia, weight loss, and cachexia associated with acquired immunodeficiency syndrome [AIDS])

Management of paraphilia (sexual deviancy), especially pedophilia and sexual sadism (Depo-Provera, 100–500 mg IM weekly to monthly—the drug has been shown to decrease erotic cravings, but sexual deviance usually returns following discontinuance of the drug)

Side effects of continuous progestin use can include:

❗ Menstrual irregularity and amenorrhea, breakthrough bleeding, and spotting

❗ Edema and weight gain

Nausea

Breast tenderness, enlargement, and secretion

Jaundice, rash, and pruritus

Headache and migraine

Mental depression

❗ Thromboembolic disorders

Vision disorders

Possible decrease in bone density with prolonged use

Cautions or contraindications for progestins (similar to cautions with estrogen) apply to:

Any condition that might be aggravated by fluid retention (e.g., asthma, seizures, migraine, and cardiac or renal dysfunction)

History of mental depression

History of thromboembolic disorders, especially with tobacco smoking

History of cerebrovascular accident

Liver disorders

Undiagnosed vaginal bleeding

Pregnancy (progestins are no longer used to treat threatened abortion because of the potential adverse effects to the fetus)

Breast, cervical, uterine, and vaginal cancers (except for palliative treatment)

Refer to Table 24-3 for a summary of the estrogens and progestins. Several different estrogen–progestin combinations are commercially available. Refer to the discussion of each individual agent.

Table 24-3 Estrogens and Progestins

Generic Name	Trade Name[a]	Dosage	Uses/Comments
Estrogens			
estradiol	Estrace	PO, intravaginal, dose varies	Menopause, prostate cancer, breast cancer, dysfunctional uterine bleeding
	Vagifem	Vaginal tabs	Atrophic vaginitis
	Estrasorb EstroGel	Topical emulsion, Transdermal gel	Only for menopausal symptoms
	Climara, Vivelle	Transdermal patch, dose varies	
	Depo-Estradiol	IM, dose varies	Female hypogonadism, prostate cancer, menopausal symptoms
conjugated estrogens	Premarin	PO, vaginal cream, parenteral; dose varies with condition symptoms	Female hypogonadism, breast and prostate cancer, menopausal symptoms
esterified estrogens	Menest	PO, dose varies with condition	Female hypogonadism, breast and prostate cancer, menopausal symptoms
Progestins			
medroxyprogesterone	Provera Depo-Provera	PO tabs IM, dose varies	Abnormal uterine bleeding, menopausal symptoms, endometrial cancer, contraception
megestrol acetate	Megace, Megace ES (625 mg/5 mL daily)	PO 160–800 mg daily in divided doses	Endometrial and breast cancer, anorexia, and cachexia of AIDS
Estrogen–Progestin Combinations			
conjugated estrogens/medroxyprogesterone	Premphase, Prempro	PO, dose varies	For menopausal symptoms
estradiol/norethindrone	CombiPatch	Transdermal, 1 patch two times per week (q3–4 days)	For female hypogonadism, menopausal symptoms
	Activella	PO, 1 tab daily	Osteoporosis prophylaxis; menopausal symptoms

Note: Because of adverse side effects, estrogen and progestin products should be administered at the lowest possible dose for effectiveness.

[a] List of trade names is not all-inclusive as the products are too numerous to mention.

Contraceptive Agents

Contraceptives are broadly referred to as a method or device serving to prevent pregnancy. The use of combination *estrogen–progestin* contraceptives as a safe and effective method of birth control has been well established. They act by suppressing the release of the pituitary hormones, FSH, and LH, thus resulting in the prevention of ovulation.

The *progestin-only* **contraceptives** prevent pregnancy by inhibiting ovulation; this is accomplished by changing the amount or thickness of the cervical mucus, thus inhibiting sperm transport and creating a thin, atrophic endometrium not conducive to sustaining the fertilized ovum. The progestin-only preparations may be indicated for those who cannot tolerate estrogenic side effects or for whom estrogen is contraindicated. Examples of these side effects are estrogen-related headaches and hypertension. Other indications include those who are breastfeeding because *progestin has no effect on lactation or nursing infants*. Young patients who have a history of noncompliance on oral contraceptives might benefit from injections or intrauterine devices (IUDs). The failure rate for progestin-only preparations ranges from 0.5% for oral agents to 0.1%–0.3% for injections and implants and 0.2%–2% for IUDs.

Uses of combined or progestin-only contraceptives include:

- Prevention of pregnancy
- Treatment and/or improvement of other medical conditions, such as fibroids and endometriosis; premenstrual dysphoric disorder; painful, heavy periods; irregular cycles; and acne

Other medical benefits of oral contraceptives include decreased incidence of ovarian cysts, ovarian or endometrial cancer, benign breast disease, and ectopic pregnancy; improved bone density during perimenopause; protective effect against pelvic inflammatory disease

Minor side effects of contraceptives include (most should resolve after a few months of use):

- Nausea
- Increased breast size and tenderness
- ❗ Fluid retention
- ❗ Weight gain or loss
- ❗ Bleeding between periods and breakthrough bleeding
- Scanty menstrual flow (considered a benefit)
- Changes in libido
- Mood changes
- Facial discoloration

Serious side effects of estrogen can include:

- ❗ Migraine headaches or headaches increasing in frequency and severity
- ❗ Severe depression
- Blurred vision or loss of vision

Cautions or contraindications for estrogen products apply to:

- Thrombophlebitis or thromboembolic disorder or history thereof
- History of cerebrovascular accident
- History of chest pain or myocardial infarction (MI)
- Known or suspected history of breast cancer or other estrogen-dependent malignancy, or preexisting cervical cancer
- Pregnancy

Major surgery with prolonged immobilization
History of liver disease or impaired liver function

In addition to the preceding precautions and contraindications, estrogen–progestin contraceptives should be used with caution in the following conditions:

Females over age 35 years and currently smoking 15 or more cigarettes a day
Migraine headaches that start after initiating oral contraceptives
Patients who are perimenopausal
Seizure disorder
Hypertension with resting diastolic above 90 mm Hg or systolic above 140 mm Hg
High cholesterol; dyslipidemia
Obesity
Diabetes mellitus
Undiagnosed vaginal bleeding
Confirmed sickle cell disease
Lactation
Oral contraceptives may accelerate the development of gallbladder disease in females who are already susceptible

Interactions of estrogen products may include the following:

Many drugs may interact with oral contraceptives and alter the effectiveness, including pain relievers, alcohol, anticoagulants, antidepressants, tranquilizers or barbiturates, corticosteroids, rifampin, antiretrovirals, asthma drugs, beta-blockers, anticonvulsants, oral hypoglycemic drugs, St. John's wort, and vitamin C.

Clinical Application

Deep Vein Thrombosis Prevention

Although most side effects of oral contraceptives (OCs) are minor and manageable, deep vein thrombosis (DVT) is a serious risk consideration for patients who chose this as a method of birth control. The patients at the highest risk are those who are over the age of 35 years, obese, and smoke (especially those who smoke >15 cigarettes/day), but all those who are taking oral birth control should be informed of this risk and made aware of potential prevention strategies. OCs should be avoided in patients with a history of DVT (and related conditions such as pulmonary embolism) and those patients needing major surgery requiring prolonged immobilization. Additionally, patients who are deemed to have a higher risk of DVT/PE should be started on an OC with 30 mcg or less of estrogen and the progestin component levonorgestrel, as these combinations show a lower DVT/PE risk than those with greater than 30 mcg of estrogen and the progestin component drospirenone. Finally, those patients who are not considered to be at a higher risk of developing DVT/PE should be informed to stay active, especially during long car rides or plane flights; maintain a healthy body mass index (BMI); monitor cholesterol and blood pressure; and avoid smoking or consider smoking cessation if applicable. Compression socks and anticoagulation therapy can also be considered as preventative options.

Patient Education

Patients taking oral contraceptives should be instructed regarding:

Using backup contraception for the first month on oral contraceptives and for the first 2 weeks with Depo-Provera

Taking the contraceptive at the same time every day (Every product comes with specific directions to follow if an oral contraceptive dose is missed. The general instruction is that the pill should be doubled up until the patient has caught up, using a backup method until the period begins. If three or more pills are missed, the patient is instructed to throw away the pack until they start their period and then begin a new pack of pills. They should stop oral contraceptives if pregnancy is suspected and stop smoking.)

Using backup contraception when taking other medicines that may alter effectiveness (refer to Interactions)

Reporting the following symptoms to the health care professional should they occur while on oral contraceptives: chest pain, shortness of breath, severe headache, dizziness, weakness, numbness, eye problems, breast lumps, or severe leg pains in the calf or thigh

The fact that oral contraceptives do not protect against HIV, AIDS, or other sexually transmitted infections (STIs)

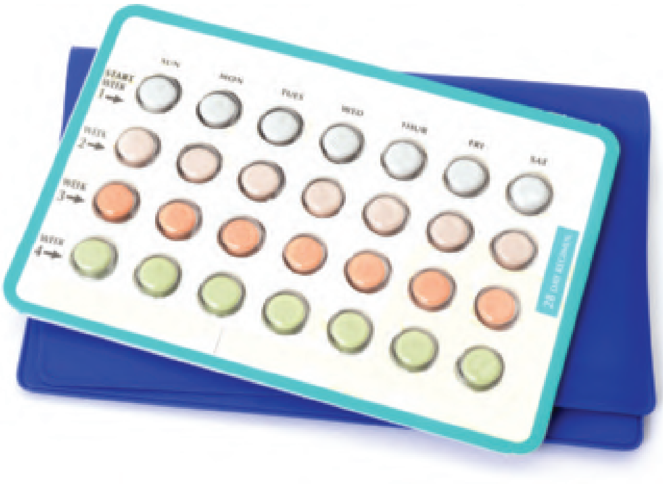
Choice of Contraceptives

This section discusses the choice of contraceptive methods by patients with various characteristics and medical conditions. Health care professionals should always consider the individual clinical circumstances of each person seeking family planning services.

Estrogen–Progestin Contraceptives

Estrogen–progestin oral contraceptives are available in several formulations and varieties of chemical preparations. They are usually classified according to their estrogen content and formulation as follows:

1. Monophasic preparations contain the same proportion of estrogen and progestin in each tablet.
2. Biphasic preparations contain two sequences of progestin doses and less than 50 mcg estrogen.
3. Triphasic preparations contain three sequences of progestin doses and less than 50 mcg estrogen. (Refer to Figure 24-2.)



Kim Reinick/Shutterstock.com.

Figure 24-2 A triphasic 21/7 oral contraceptive. It is designed to mimic natural hormonal release in the body and has three different doses of oral contraception (one week each) and a fourth week that is a hormone-free interval.

4. Four-phasic preparations contain four sequences of estradiol valerate, a synthetic estrogen, and two (middle) sequences of the progestin dienogest.

The biphasic and triphasic formulations are intended to deliver the hormones in a manner similar to physiological processes.

Extended- or continuous-cycle oral contraceptives differ from traditional 21/7 products by decreasing or eliminating the hormone-free interval (HFI). Consecutive days of HT may extend to 84 or 365 days, with the HFI shortened to 0, 2, or 4 days instead of the typical 7-day interval. Reasons for considering an extended- or a continuous-cycle product include decreasing the typical menstrual symptoms (especially headaches) experienced during the HFI; improving efficacy in patients who forget to restart the pill; and patient preference to decrease the frequency of menstrual-like bleeding, although breakthrough bleeding is more likely.

Choice of a particular contraceptive will be made after considering the patient's history, hormone-related side effects, prior use, and desired effect. In general, whenever possible, start on monophasic regimens with the smallest dose of estrogen (20 mcg for most patients) and progestin (levonorgestrel or norethindrone) that is compatible with a low failure rate and meets the individual needs of the patient.

Broad categories are listed in Table 24-2. Individual oral contraceptives are too numerous to mention in their entirety; however, a few examples in each category are included.

Progestin-Only Contraceptives

These preparations are recommended for patients who do not tolerate estrogen, or in whom it is contraindicated. The choice of the method of delivery (i.e., oral tablets, injection, or IUD) should be made to appropriately accommodate the patient's needs and compliance. It should be noted that use of Depo-Provera injections may be considered among the risk factors for development of osteoporosis (partially reversible upon discontinuation).

Progestin-Containing Intrauterine Device (IUD)

Mirena contains a reservoir of levonorgestrel, a synthetic progestin. It releases small amounts of progesterone daily, providing 5 years of continuous contraception protection. The mechanism of action of the IUD is not fully understood, but it is generally thought to have an inhibitory effect on sperm migration, change ovum transport, and alter the endometrium. The progestin in the IUD is thought to offer support to all these actions.

There are many considerations, precautions or contraindications, and side effects that must be addressed when considering the IUD as a method of contraception, but they are too numerous to mention here. The purpose of including the IUD here is to inform the reader that it is one of several delivery systems that use progestin as a contraceptive drug.

Estrogen- and Progestin-Containing Vaginal Rings

Birth control rings are a safe and convenient birth control method that are used by inserting inside the vagina a small, flexible ring that releases hormones (estrogen and progestin). There are two birth control rings currently available (NuvaRing and Annovera). Nuvaring lasts for up to five weeks, but is generally removed monthly to allow for a regular period to occur. Annovera lasts for one year, and is removed every three weeks to allow a period to occur. Like other combined contraceptives, the rings work to prevent ovulation.

Postcoital Contraception

Although the use of combined estrogen–progestin contraceptive pills as a means of emergency or postcoital contraception is not without risk, it is an available option to those who are exposed to the unintentional risk of pregnancy. This includes such circumstances as a broken condom, rape, defective barrier methods, lost or forgotten oral contraceptives, or any other method that is not available at the time that it is needed. Emergency contraception options in the United States include estrogen and progestin combinations, progestin-only products, and a progesterone agonist/antagonist.

When using postcoital or morning-after contraception, it is essential that the patient's history is reviewed, that they are informed of the risks and benefits of postcoital contraception, and that they give informed consent. There is no medical condition for which the risks of emergency contraception use outweigh the benefits; therefore, emergency contraception *can be taken* by patients with contraindications to conventional oral contraceptives. Emergency contraception should *not* be used as a regular method of birth control and is not as effective as other forms of contraception.

Patients already on certain estrogen–progestin combination oral contraceptives can take a higher dose of their regular pill for use as emergency contraception if administered within 72 h of unprotected intercourse. Typical dosages for oral contraceptives in this instance are Lo/Ovral, Seasonale, and Triphasil, four tablets taken in two doses, 12 h apart, for a total of eight tablets. Side effects, which include nausea and vomiting, headache, and breast tenderness, usually subside within 1 or 2 days after treatment. Again, it must be noted that postcoital contraception must be administered within 72 h of unprotected intercourse and is more effective the sooner it is taken after having unprotected sex.

Next Choice is an emergency contraceptive formulation containing two tablets of the progestin levonorgestrel; Plan B One-Step contains one tablet. Progestin-only emergency contraception is more effective and causes less nausea and vomiting than the oral contraceptive combinations. The first tablet should be taken as soon as possible, but within 72 h after having unprotected intercourse. For Next Choice only, the second tablet must be taken 12 h after the first. Taken within 3 days of sexual intercourse, these progestin-only medications prevent ovulation or, if ovulation has already occurred, *block implantation of the fertilized egg*.

Ulipristal acetate (Ella) is a progesterone agonist/antagonist and is effective for the prevention of pregnancy when taken up to 5 days after unprotected intercourse. It most likely works by delaying or inhibiting ovulation. Ulipristal is available by prescription only and is not intended for more than one episode of unprotected intercourse in a menstrual cycle. The recommended dose is one tablet as soon as possible within 5 days; if vomiting occurs within 3 h of taking the tablet, consider repeating the dose. Side effects include headache, vomiting, abdominal pain, and dysmenorrhea.

Refer to Table 24-4 for a summary of contraceptive agents.

Table 24-4 Contraceptive Agents

Generic Name	Trade Name[a]	Dosage	Uses/Comments
Monophasic Preparations			
50 mcg estrogen	Necon 1/50 Ovcon-50	PO	Contain the same proportion of estrogen and progesterone in each tablet
35 mcg estrogen	Norinyl 1/35 Ortho-Novum 1/35 Brevicon	PO	
30 mcg estrogen	Lo/Ovral	PO	
	Seasonale	PO	Extended-cycle regimen
	Yasmin	PO	
20 mcg estrogen	YAZ	PO	Extended-cycle regimen
	Lybrel	PO	Continuous-cycle regimen
	Ortho Evra	Transdermal	1 patch q7days for 3 weeks per cycle
Biphasic Preparation—2 Sequences Progestin/1 Part Estrogen			
	Seasonique	PO	Extended-cycle regimen
	Mircette	PO	
Triphasic Preparation—3 Sequences Progestin/One Part Estrogen			
	Trivora	PO, dose varies	
	Ortho-Novum 7/7/7	PO	
	Ortho-Tri-Cyclen	PO	
Four-Phasic Preparation—Four Sequences Estrogen/Two Sequences Progestin			
Dienogest and estradiol	Natazia	PO, dose varies	Effective for heavy menstrual bleeding
ethinylestradiol and levonorgestrel	Quartette	PO, dose varies	Effective for heavy menstrual bleeding
Progestin-Only Preparations			
	Ortho Micronor	PO	"Mini-pill"
	Depo-Provera	IM, 150 mg q3m	
	Mirena	Intrauterine device (IUD)	
Postcoital Contraception			
levonorgestrel	Lo/Ovral, Seasonale	PO, 4 tabs q12h for total of 8 tabs (must be administered within 72 h)	With norgestrel- and levonorgestrel-containing combination products (dose varies with other products)
	Next Choice	PO, 1 tab q12h for a total of 2 tabs (within 72 h)	Available OTC for 17+ years; Rx only for ≤16 years old
	Plan B One-Step	PO, 1 tab single dose (within 72 h)	Now available OTC with no age restrictions
ulipristal	Ella	PO, 1 tab single dose (within 120 h)	Rx only

Note: Because of adverse side effects, estrogen and progestin products should be administered at the lowest possible dose for effectiveness.

[a] List of trade names is not all-inclusive, as the available oral contraceptives are too numerous to mention.

Patient Education

Patients taking estrogen, progesterone, or combinations of the two should be instructed regarding:

Importance of following the prescribed schedule with contraceptives

Taking with or after evening meal or at bedtime, at the same time every day

The fact that these products do not protect against HIV infection or other sexually transmitted diseases (STDs)

Minor adverse effects of contraceptives (for example, edema, weight gain, and nausea)

Possible serious side effects and the importance of reporting any signs of cardiovascular or kidney disorders, liver or gallbladder dysfunction, rash, jaundice, GI symptoms, visual disturbance, severe headache, breast lumps, irregular vaginal bleeding, shortness of breath, and chest or calf pain

Increased risk of stroke or myocardial infarction (MI) for smokers

Regular breast self-examination

Complete physical examination, including Pap test, at least yearly

Avoidance of all estrogen or progestin products if pregnant (however, note that the American Academy of Pediatrics considers both estrogens and progestins to be generally compatible with breastfeeding).

Drugs for Labor and Delivery

In addition to the hormones secreted by the anterior pituitary gland, there is also a hormone secreted by the posterior pituitary lobe: **oxytocin**. This hormone stimulates the uterus to contract, thus inducing childbirth. Oxytocin also acts on the mammary glands to stimulate the release of milk. Synthetic chemicals used to stimulate uterine contractions are called oxytocics and include oxytocin and prostaglandin E_1 and E_2.

The goal of labor induction at term is to facilitate the vaginal delivery of a healthy infant. Induction of labor may be required for pregnancies that go beyond term, those in which premature rupture of the membranes occurs, or pregnancies in which there are indications in those who are pregnant or the fetus for early delivery.

Oxytocin

Uses of oxytocin (IV infusion of dilute solutions slowly and at a carefully monitored rate) include:

Inducing labor with at-term or near-term pregnancies associated with hypertension (e.g., preeclampsia, eclampsia, or cardiovascular or renal disease), diabetes in those who are pregnant, or uterine fetal death at term

Stimulating uterine contractions during the first or second stages of labor if labor is prolonged or if dysfunctional uterine inertia occurs

Pelvic adequacy and other conditions in both those who are pregnant and the fetus must be evaluated carefully prior to the induction of labor. Cesarean section may be preferable and safer in some instances.

Side effects of oxytocin are dose related and can be serious, even resulting in death of those who are pregnant or the fetus. *Extreme caution* with administration and *constant monitoring of both those who are pregnant and the fetus* are required to prevent dangerous side effects such as:

❗ Tetanic contractions with the risk of uterine rupture

Cervical lacerations

- ❗ Abruptio placenta
- Impaired uterine blood flow
- Amniotic fluid embolism
- ❗ Fetal trauma, including intracranial hemorrhage or brain damage
- ❗ Fetal cardiac arrhythmias, including bradycardia, tachycardia, and premature ventricular contractions
- ❗ Fetal death due to asphyxia

With large amounts of oxytocin, watch for:

- ❗ Severe hypotension
- ❗ Tachycardia and arrhythmias
- ❗ Postpartum hemorrhage
- Subarachnoid hemorrhage
- Hypertensive episodes

Cautions or contraindications for oxytocin apply to:

- Elective induction of labor merely for physician or patient convenience, which is *not* a valid indication for oxytocin use
- Cephalopelvic disproportion and unfavorable fetal position or presentation
- Uterine or cervical scarring from major cervical or uterine surgery
- Fetal distress when delivery is not imminent
- Placenta previa, prolapsed cord, and multiparity
- Prolonged use with eclampsia

Prostaglandins

Prostaglandins are released as a natural part of the cervical ripening process. Prostaglandins that cause the contraction of the myometrial muscle include dinoprostone or prostaglandin E_2 (Prostin E_2, Cervidil, Prepidil), the oral synthetic prostaglandin E_1 analog, misoprostol (Cytotec), and the prostaglandin F2-alpha analog carboprost (Hemabate). All prostaglandins stimulate smooth muscle in the GI tract, accounting for the GI side effects experienced.

Uses of dinoprostone intravaginal gel or vaginal insert include:

- Cervical ripening

Uses of dinoprostone vaginal suppositories or carboprost injection include:

- Therapeutic abortion in the second trimester (beyond the 12th week)
- Uterine evacuation in cases of intrauterine fetal death in late pregnancy; benign hydatidiform mole; or fetuses with acephaly, erythroblastosis fetalis, or other congenital abnormalities *incompatible with life*

Uses of carboprost injection include:

- Treatment of postpartum bleeding because of uterine atony that is unresponsive to conventional management, including oxytocin IV, uterine massage, uterine manipulation, and injectable ergot preparations

Side effects of prostaglandins can be minimized by the administration of a prior test dose and symptomatic treatment of such effects as:

- ❗ GI hypermotility, including nausea, vomiting, and diarrhea (decreased by premedication with antiemetics and antidiarrheal agents)
- ❗ Bradycardia, hypotension, hypertension, and arrhythmias
- ❗ Dizziness, syncope, flushing, and fever
- ❗ Bronchospasm, including wheezing, dyspnea, chest constriction, and chest pain
- Cervical laceration or uterine rupture (less common)
- Retained placenta (less common)

Cautions or contraindications for prostaglandins include:

- Use only by trained physicians in a hospital where intensive care and surgical facilities are available
- Contraindicated with a history of pelvic surgery, uterine fibroids, cervical stenosis, and acute pelvic inflammatory disease
- Caution with asthma, hypertension, and cardiovascular or renal disease
- Previous history of Cesarean section

Mifepristone (RU-486)

Mifepristone (Mifeprex) is an antiprogesterone drug that is used to terminate an unwanted pregnancy (in conjunction with misoprostol). There are detailed requirements (including informed consent) to ensure that those who are pregnant fully understand the process. The drug is sold directly to trained physicians and is not available in pharmacies. Patient education (*Mifepristone Medication Guide*) is very important for the proper administration of this drug.

Mifepristone is for use only very early in pregnancy—within 49 days from the beginning of the last menstrual period. Mifepristone blocks the action of progesterone, a hormone essential for maintaining pregnancy. Without progesterone, the uterine lining thins, so the embryo cannot remain implanted and grow. It requires three visits to a qualified physician to complete the treatment:

1. At the first visit, the physician will determine the gestational status. If the patient qualifies for the procedure, they must sign an informed consent agreeing to the necessary visits. They will then receive three mifepristone pills to be taken by mouth.
2. The second step requires the patient to swallow a second drug two days later to fully detach the embryo from the uterus and expel it. Misoprostol (Cytotec) causes uterine contractions with miscarriage-like cramping and bleeding.
3. The third step requires a follow-up visit to the physician within two weeks to make sure the abortion is complete. In case of hemorrhage, it might be necessary to consult the physician sooner. Studies have shown that mifepristone is 77–92% effective in terminating pregnancy. However, in some cases, a curettage of the uterine cavity is required to remove any remaining products of conception.

Side effects of mifepristone can include:

- ! Diarrhea and nausea
- ! Uterine hemorrhage in about 5% of patients
- Infection if the embryo is not completely expelled
- A malformed child if the second and third steps are not completed

Cautions or contraindications of mifepristone apply to:

- Ectopic pregnancy
- Any time after 49 days from the beginning of the last menstrual period
- Current long-term corticosteroid therapy
- Bleeding disorders
- Current anticoagulant therapy

The Food and Drug Administration (FDA) recently approved mifepristone (Korlym) for the treatment of hyperglycemia in patients with Cushing's syndrome who have type 2 diabetes and are not candidates for or responding to prior surgery. Korlym is contraindicated in pregnancy.

Methylergonovine

The semisynthetic ergot alkaloid methylergonovine is used for the prevention and treatment of postpartum and postabortion hemorrhage.

Side effects of methylergonovine occur most commonly when administered IV undiluted or too rapidly, or in conjunction with regional anesthesia or vasoconstrictors, and can include:

- ! Nausea and vomiting
- ! Dizziness, headache, diaphoresis, palpitation, dyspnea, and arrhythmias
- Hypertension (more common) or hypotension
- Numbness and coldness of extremities with overdose (peripheral vasoconstriction)
- Seizures with overdose

Cautions or contraindications for methylergonovine include:

- When administered during the third stage of labor, may lead to retained placenta
- Contraindicated with cardiovascular disease, especially hypertension, and with hepatic and renal impairment
- Patients with preeclampsia or eclampsia

Terbutaline

Terbutaline, although classified as a bronchodilator drug primarily used for pulmonary disorders, is also used with careful monitoring in the management of preterm labor. Its sympathomimetic action inhibits uterine contractions (**tocolysis**) by smooth muscle relaxation. Although the manufacturer does not recommend its use for preterm labor, it is used off-label for this purpose in urgent situations with careful monitoring in the hospital setting. It is available for oral, IV, or subcutaneous administration but is only used subcutaneously or intravenously for this condition.

Side effects of terbutaline include:

❗ *In those who are pregnant:* nervousness, tremors, increased heart rate, headache, nausea, vomiting, hypotension, heart palpitations, cardiac arrhythmias, myocardial ischemia, and metabolic abnormalities (hyperglycemia and hypokalemia)

In the fetus: tachycardia, hypotension, hyperbilirubinemia, hypoglycemia, hypocalcemia, and intraventricular hemorrhage.

Caution with terbutaline applies to:

Monitoring the patient closely for signs of pulmonary edema; should not be used in patients with hypertension, cardiac disease, hyperthyroidism, diabetes, or history of seizures.

Cautions or contraindications for terbutaline (black-box warning) apply to:

Prolonged tocolysis (use beyond 48–72 h) for terbutaline administered by injection or by continuous infusion pump because of the potential for serious cardiovascular events and death in those who are pregnant.

Magnesium Sulfate

Preeclampsia is characterized by new-onset hypertension, edema, and proteinuria during pregnancy. Patients become eclamptic when they develop new-onset grand mal seizures in the presence of preeclampsia and require immediate medical intervention. Treatment of severe preeclampsia or eclampsia consists of controlling elevated blood pressure and utilizing magnesium sulfate injections for the prevention and control of seizures.

Magnesium sulfate acts by depressing the central nervous system (CNS), blocking neuromuscular transmission, and causing cerebral vasodilation, thus producing anticonvulsant effects. It has also been used in the management of uterine tetany associated with the use of oxytocic agents. Magnesium sulfate also acts peripherally, producing vasodilation and lowering blood pressure. Patients receiving this drug must be monitored closely for vital signs and reflexes.

Side effects of magnesium sulfate, which can be serious and even fatal, can include:

❗ Flaccid paralysis and CNS depression

❗ Circulatory collapse, cardiac depression, and cardiac arrest

❗ Pulmonary edema and fatal respiratory paralysis

Flushing, sweating, and hypotension

Fetal toxicity at high doses (rare with proper use and monitoring)

The antidote for overdose of magnesium sulfate (e.g., respiratory depression or heart block) is IV administration of calcium gluconate.

Cautions or contraindications when using magnesium sulfate apply to:

Impaired renal function

Heart block or myocardial damage

Prolonged use because of potential respiratory depression in the neonate

Refer to Table 24-5 for a summary of drugs for labor and delivery.

Table 24-5 Drugs for Labor and Delivery

Generic Name	Trade Name	Dosage	Comments
Oxytocics[a]			
methylergonovine	Methergine[b]	PO, IM; dosage varies	For postpartum hemorrhage
oxytocin	Pitocin	IV, IM	For the induction of labor and for postpartum hemorrhage
Prostaglandins			
dinoprostone	Prostin E2	Vaginal supp, 20 mg	For therapeutic abortion
	Cervidil	Vaginal insert, 10 mg	For cervical ripening
	Prepidil	Intravaginal gel, 0.5 mg	For cervical ripening
misoprostol	Cytotec	Tablets	For pregnancy termination (used with mifepristone)
carboprost	Hemabate	IM, dose varies	For refractory postpartum bleeding, pregnancy termination
Tocolytic[c]			
terbutaline		IV, SQ, dose varies	Short-term for premature labor (PO now contraindicated for this use)
Treatment for Preeclampsia or Eclampsia			
magnesium sulfate		IM, IV; dosage varies	Monitor for respiratory complications

[a] Stimulate uterine contractions.

[b] This brand name is no longer marketed, but the name may still be commonly used.

[c] Inhibit uterine contractions in preterm labor.

Other Gonadotropic Drugs

Drugs classified as analogs of *gonadotropin-releasing hormones* (GnRHs) act in the pituitary gland to suppress ovarian and testicular hormone production and inhibit estrogen and androgen synthesis. Leuprolide (Lupron) has been used as an antineoplastic agent to inhibit the growth of hormone-dependent tumors. It has been used to reduce the size of the prostate and inhibit prostatic tumor growth. Lupron has also been used following other therapies, for example, mastectomy, radiation, and/or other antineoplastic drugs to treat breast cancer. It is sometimes combined with the antiestrogen drug tamoxifen in the treatment of breast cancer.

GnRH analogs that inhibit gonadotropin secretion, for example, Lupron and Synarel, are used in the management of endometriosis. Endometriosis is a condition where endometrial tissue develops outside the uterus, causing pelvic or lower back pain. GnRH analogs inhibit ovulation and stop menstruation (similar to what occurs in menopause), thereby providing pain relief and a reduction in endometriotic lesions. Lupron is administered as a monthly (3.75 mg) or trimonthly (11.25 mg) IM injection. Synarel is administered as a nasal spray. Treatment with either is limited to 6 months. Both drugs appear to be better tolerated than the androgen danazol in the treatment of endometriosis.

Side effects of the GnRH agonists (menopausal symptoms) can include:

- ❗ Hot flashes and diaphoresis
- Vaginal dryness and vaginitis

Headache and insomnia

Emotional or mood swings and reduced libido

Weight gain or loss and peripheral edema

Nasal congestion or irritation with Synarel

Acne

Cautions or contraindications include the following:

Not to be considered effective as a contraceptive; the patient should use a backup barrier method

Pregnancy or lactation

Diabetes (monitor the blood glucose level carefully)

Prolonged use creates a hypoestrogenic state that may lead to an increased risk of loss of bone density (monitor bone mineral density)

Patients must be fully informed of the benefits and risks of the use of GnRH analog drugs, and, generally speaking, the therapeutic values should outweigh any potential risks. Patient compliance is enhanced with adequate patient education, counseling, and support.

Refer to Table 24-6 for a summary of other gonadotropin-associated drugs.

Table 24-6 Other Gonadotropin-Associated Drugs

Generic Name	Trade Name	Dosage	Comments
nafarelin acetate	Synarel	Nasal spray, 200 mcg/spray; alternate nares, dose varies	For endometriosis, treatment not to exceed 6 months
leuprolide acetate	Lupron Depot, Eligard	IM, SQ, dose varies	For endometriosis, some cases of infertility, treatment not to exceed 6 months; also for prostate cancer

Case Study A

Reproductive System Drugs

A 24-year-old patient has been experiencing painful and heavy-flow menses. At a recent visit to the gynecologist, they were diagnosed with endometriosis.

1. The physician writes a prescription for an oral contraceptive containing estrogen and progestin and explains that this might help the patient's condition by:
   a. Increasing the frequency of ovulation
   b. Increasing the amount or thickness of cervical mucus
   c. Decreasing the amount of pituitary hormones released
   d. Creating a thin, atrophic endometrium not conducive to sustaining a fertilized ovum

2. The physician explains that the patient might experience some minor side effects that should resolve after a few months of use. Which of the following is one of these possible side effects?
   a. Constipation
   b. Weight gain
   c. Painful joints
   d. Pelvic pain

3. Prior to writing the prescription for the contraceptive, the physician reviews the patient's medical history. This is important because contraceptives are contraindicated in patients with a history of:
   a. Asthma
   b. Thrombophlebitis
   c. Peanut allergy
   d. Breast augmentation

4. The nurse instructs the patient on how to take the contraceptive. Which of the following instructions is most likely to be included in the teaching plan?
   a. Use a backup contraceptive for 3 months.
   b. Take the oral contraceptive at the same time each day.
   c. Note that oral contraceptives protect against HIV.
   d. Take a drug holiday after taking the contraceptive for 6 months.

5. What symptom would be most important for the patient to report to their physician after starting the oral contraceptive?
   a. Chest pain
   b. Urinary frequency
   c. Breast tenderness
   d. Rash on chest

Case Study B

Reproductive System Drugs

A patient is in the 31st week of pregnancy and has developed hypertension, 3+ edema in their ankles, and proteinuria. The obstetric (OB) physician is concerned that the patient may develop new-onset grand mal seizures related to eclampsia. The patient is admitted to the hospital and started on IV magnesium sulfate.

1. The patient is reluctant to start on the IV because they are concerned about the drug magnesium sulfate. The physician explains that the medication is necessary for their condition and will produce an anticonvulsant effect by:
   a. Peripheral vasoconstriction
   b. An increase in circulatory volume
   c. Depressing the CNS and thereby causing cerebral vasodilation
   d. The induction of bradycardia and a subsequent reduction in blood pressure

2. The nurse notes a physician order for an antidote in case of an overdose of magnesium sulfate. The drug that will be on hand in case of an overdose is:
   a. Calcium carbonate
   b. Glucagon
   c. Calcium gluconate
   d. Carboprost

3. Extreme caution should be exercised when administering magnesium sulfate because of its potential effects on the fetus This includes the potential for:
   a. Hypotension
   b. Increased risk of seizure
   c. Respiratory depression
   d. Hypertension

4. What is one of the serious side effects of magnesium sulfate?
   a. Hypertension
   b. Flaccid paralysis
   c. Status asthmaticus
   d. Severe dehydration

5. While the patient is receiving IV magnesium sulfate, they will be monitored closely for:
   a. Vital signs and reflexes
   b. Blood glucose levels
   c. Hematocrit and hemoglobin
   d. Creatinine clearance

Chapter Review Quiz

Match the medications in the first column with the conditions they are used to treat. Conditions may be used more than once.

Medication

1. ___ Premarin
2. ___ Megace
3. ___ Depo-Testosterone
4. ___ Danocrine
5. ___ Covaryx
6. ___ terbutaline
7. ___ Cialis
8. ___ Levitra
9. ___ Pitocin

Condition

a. Endometriosis
b. Menopausal symptoms
c. Prostate cancer
d. Erectile dysfunction
e. Hypogonadism
f. Uterine inertia in labor
g. Infertility
h. Preterm labor
i. Cachexia of AIDS

Choose the correct answer

10. What possible side effect should a patient taking tadalafil report to a physician?

a. Insomnia
b. Vision abnormalities
c. Constipation
d. Tingling in the feet

11. Which category of drugs has serious interactions with PDE inhibitors?

a. Nitrates
b. Anti-inflammatories
c. Muscle relaxants
d. Hypoglycemic agents

12. Patients with a uterus should not use estrogen-alone therapy because it puts them at risk for which of the following?

a. Blood clots
b. Uterine cancer
c. Stroke
d. Osteoporosis

13. Estrogen therapy (i.e., estrogen alone) has been associated with an increased risk of endometrial cancer. Estrogen combined with which agent reduces this risk?

a. Testosterone
b. Androgens
c. Progestin
d. Progesterone agonist

14. A contraceptive preparation containing two sequences of progestin doses and less than 50 mcg of estrogen is called:

a. Monophasic
b. Biphasic
c. Triphasic
d. Four-phasic

15. Dinoprostone intravaginal gel or vaginal insert is indicated for:

a. Premature labor
b. Therapeutic abortion
c. Induction of labor
d. Cervical ripening

16. Oxytocin should be avoided for patients with a history of:

a. Miscarriage
b. Diabetes mellitus
c. Endometriosis
d. Placenta previa

17. A side effect of methylergonovine, given for the treatment of postpartum hemorrhage, can include:

a. Fever
b. Nausea and vomiting
c. Urinary retention
d. Peripheral vasodilation

18. Which of the following drugs is used primarily for pulmonary disorders but can also be used for the management of preterm labor?

a. Oxytocin
b. Carboprost
c. Terbutaline
d. Misoprostol

19. Side effects of terbutaline in those who are pregnant include:

a. Hyperglycemia
b. Hypoglycemia
c. Hyperthryoidism
d. Hyperkalemia

20. Side effects of terbutaline in the fetus include:

a. Hypercalcemia
b. Hypobilirubinemia
c. Tachycardia
d. Intra-abdominal bleeding

21. Extreme caution is required with the administration of oxytocin, along with constant monitoring of both those who are pregnant and the fetus, to prevent which side effect?

a. Cervical stricture
b. Maternal desaturation
c. Maternal seizures
d. Uterine rupture

Chapter 25

Anti-Infective Drugs

Key Terms and Concepts

Adverse reactions
Aminoglycosides
Anaphylaxis
Antifungal
Antiretroviral (ARV) agents
Antituberculosis agents
Antiviral agent
Broad spectrum
Carbapenems
Cephalosporins
Culture and sensitivity (C&S) tests
Direct toxicity
Empiric
Macrolides
Opportunistic infections
Penicillins
Quinolones
Resistance
Shared Clinical Decision Making (SCDM)
Sulfonamides
Superinfection
Tetracyclines
Urinary anti-infectives
Vaccines

Objectives

Upon completion of this chapter, the learner should be able to:

1. Identify indications, side effects, precautions and contraindications, and interactions common to each category of anti-infectives.
2. Explain the unique features of patient education appropriate for each category of anti-infective.
3. Describe the general instructions that should be given to every patient undergoing anti-infective therapy.
4. Explain the mechanism for resistant organism development and its significance.
5. Explain the role of vaccines in preventing diseases.

According to the U.S. Centers for Disease Control and Prevention (CDC), nearly 20% of visits to office-based physicians and hospital outpatient departments are made annually for the treatment of infections and parasitic diseases. The first step in treatment is identifying the causative organism and the specific medication to which it is sensitive. **Culture and sensitivity (C&S) tests** will be ordered (e.g., wound, throat, urine, or blood), based on symptoms (refer to Figure 25-1). It is imperative to obtain the appropriate specimen before administering medication. Results of C&S tests may not be available for 24–48 h. In the meantime, depending on the clinical condition of the patient, the physician may order an **empiric** (best guess based on history) anti-infective regimen that would likely be active against the organisms encountered at the given site of infection (e.g., brain, lung, skin).

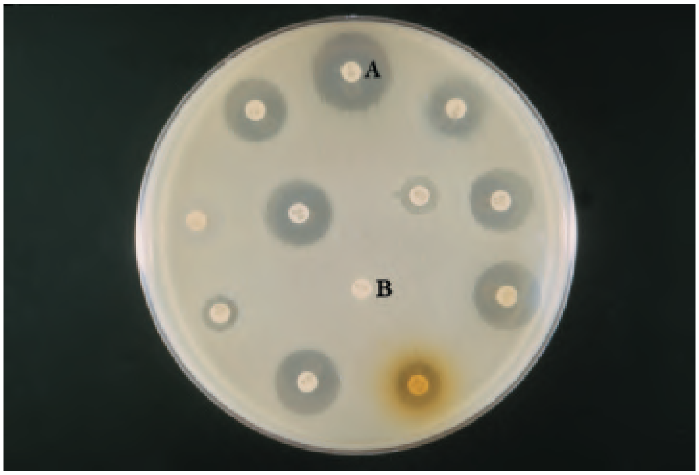


Figure 25-1 An agar plate where the organism has been cultured (grown) with several different antibiotic-containing paper disks placed on the "lawn" of organisms. Note the varying zones of inhibition or no growth. (A) A highly sensitive organism that is killed by the antibiotic. (B) A resistant organism that is not affected.

Courtesy of the Centers for Disease Control and Prevention

Resistance

Sometimes organisms build up **resistance** to drugs that have been used too frequently or improperly, and then the drugs are no longer effective. An example of an organism resistant to most antibiotics is methicillin-resistant *Staphylococcus aureus* (MRSA). Vancomycin IV is one of a small number of drugs effective against MRSA, along with Teflaro, which is a newer cephalosporin.

Some strains of enterococci have become resistant to most antibiotics, including vancomycin. Infections caused by vancomycin-resistant enterococci (VRE) such as bacteremia, endocarditis, and urinary tract infections (UTIs) can be very difficult to treat. Treatment options are limited, and mortality rates tend to be high, but scientists are continually working to develop new antibiotic therapies to combat this issue. As you progress through this chapter, notice newer drugs that have been designed to combat strains that have developed resistance to traditional therapy. Resistance to antiviral and antifungal agents is also an important clinical problem. *Candida* species resistant to fluconazole are a growing problem in many health care institutions as well because of widespread use of this antifungal agent.

Anti-infective resistance is caused by many factors. Therefore, the strategies needed to combat the problem are also complex. Effective strategies include better patient and physician *education* on appropriate anti-infective use, accurate diagnosis, and targeted treatment of infections. Strict adherence to *preventive measures,* such as routine handwashing and alcohol wiping between patient visits along with rapid isolation of patients with resistant infections, is also extremely important.

Selection of anti-infective drugs is based on several factors:

1. ***Site of the infection.*** This helps determine the initial empiric anti-infective regimen.
2. ***Status of hepatic and/or renal function.*** Lower doses or alternative drugs might be indicated with impairment.

3. ***Age of the patient.*** Some anti-infectives are more toxic to children or older patients. Lower doses or alternative drugs might be indicated.
4. ***Pregnancy or lactation.*** Some anti-infectives, for example, tetracycline and streptomycin, can cross the placenta and cause damage to the developing fetus. Others can be carried in breast milk and can cause toxicity to the infant.
5. ***Likelihood of organisms developing resistance.*** Sometimes a combination of drugs is used to decrease the chance of the organism developing resistance to a single drug. Examples of combination therapy include sulfamethoxazole and trimethoprim combined to treat UTIs. Another example is the combination of three or more drugs to treat tuberculosis.
6. ***Known allergy to the anti-infective drug.*** In such cases, an alternative should be used.

Adverse Reactions

Adverse reactions to anti-infectives are divided into three categories:

1. ***Allergic hypersensitivity.*** This is an over-response of the body to a specific substance. A *mild* reaction with only rash, urticaria (hives), or mild fever is usually treated with corticosteroids or antihistamines, and the medication is *discontinued*. Sometimes severe reactions occur. *Severe* reactions may be manifested as **anaphylaxis**, a sudden onset of dyspnea, chest constriction, shock, and collapse. Unless treated promptly with epinephrine, corticosteroids, and CPR (cardiopulmonary resuscitation), death may result.
2. ***Direct toxicity.*** Results in tissue damage, such as ototoxicity (hearing difficulties or dizziness), nephrotoxicity (kidney problems), hepatotoxicity (liver damage), and other issues. Sometimes the damage can be permanent, or it may be reversible when the medication is discontinued; therefore, immediately discontinuing the medication at the first sign of toxicity is crucial.
3. ***Indirect toxicity, or superinfection.*** Manifested as a new infection as a result of killing the normal flora in the intestines or mucous membranes, especially with broad-spectrum antibiotics, and therefore allowing colonization of these areas with different resistant bacteria or fungi. Symptoms of superinfections can include diarrhea, vaginitis, stomatitis, or glossitis. Treatment consists of taking antifungal medications, including buttermilk or yogurt in the diet, or administering probiotics to help restore normal intestinal flora. Probiotics, available over the counter (OTC), are also used prophylactically to prevent superinfections, especially in patients with severe colitis or in patients with a history of such infections.

Immunizations

Information regarding **vaccines** and immunizations changes from time to time, and requirements may vary by state, territory, or country. The most up-to-date information regarding vaccines, immunization recommendations, and requirements can be obtained on the CDC website, http://www.cdc.gov/vaccines. Vaccine recommendations are established by the Advisory Committee on Immunization Practices (ACIP), a subdivision of the CDC. New recommendations and subsequent updates to existing recommendations are carefully considered by a panel of experts and voted on, with the final sign-off coming from the CDC Director. Vaccine recommendations change when new products come to the market (e.g., RSV vaccines or a pneumococcal vaccine such as Prevnar 20 or CAPVAXIVE) or when new data become available on the efficacy or safety of existing vaccines and when disease epidemiology changes (e.g., COVID-19 vaccines). Vaccine recommendations can be universal, meaning they are recommended for everyone in a certain group (e.g., age, disease state) or risk-based, meaning they may be recommended for some people in a group based on personal risk. Universal vaccine recommendations are also called "routine," while risk-based recommendations are sometimes referred to as **Shared Clinical Decision Making (SCDM)** recommendations. Figure 25-2 provides examples of some common routine and SCDM recommendations.

Universal (routine)	Risk-based (SCDM)
Age ≥50: Zoster vaccine	Age 27—45: HPV vaccine
Age 11—26 years: Human Papillomavirus (HPV) vaccine	Age ≥60: Hepatitis B vaccine
Age ≥65 or adults with diabetes: Pneumococcal vaccine	

Figure 25-2 Examples of Universal vs. risk-based Vaccine Recommendations (Examples only, not an inclusive list).

One long-standing recommendation of the CDC is that everyone ≥6 months of age receive an annual influenza vaccine in the fall and winter months. It is important to get a dose every year because the annual influenza vaccine is reformulated each year to include the strains of the virus that are most likely to be circulating during flu season. More recently, COVID-19 vaccines have adopted this model, and it is expected that they will also be reformulated each year with a single annual dose being sufficient for most people (immunocompromised are recommended to receive additional dose(s)). Please note that vaccines for most other diseases are not updated annually. Instead, new products replace older products (e.g., Prevnar 20 replaced Prevnar 13, which replaced Prevnar 7).

There are many diseases that are considered to be vaccine-preventable, including pneumonia, shingles (herpes zoster), influenza, COVID-19, MMR (measles, mumps, and rubella), chickenpox (varicella), tetanus, pertussis, diphtheria, hepatitis A and B, human papillomavirus (HPV), respiratory syncytial virus (RSV), meningococcal disease, mpox (formerly known as monkeypox), and haemophilus influenzae type B (HiB). A full immunization schedule for adults can be found in Figure 25-3. It should be noted that many other vaccines exist for the prevention of diseases not prevalent in the United States. These vaccines are not included on the CDC's immunization schedule, but are often recommended for travelers to foreign countries. Examples of these "travel vaccines" include those that protect against yellow fever (YF), Japanese encephalitis (JE), cholera, typhoid, and rabies.

Clinical Connection

Have you ever wondered why vaccines are recommended to be administered to a certain group of people? In most cases, recommendations target older adults because of the natural decline of the immune system that comes with aging, but this is not always the case. For example, two vaccines (Abrysvo and Arexvy) have recently become available to protect both older adults and unborn infants from severe RSV. Both vaccines are recommended for all adults 75 years of age and older, and also those 60-74 if they have a high-risk factor as defined by the CDC/ACIP. The Abrysvo vaccine is also recommended for those who are pregnant during weeks 32 through 36 of pregnancy, administered September through January. Antibodies created by those who are pregnant are passed onto the fetus, thus providing protection at birth and through the early months of life. Another vaccine that acts in this same manner, and is therefore recommended for use each time a person becomes pregnant, is the pertussis vaccine (formulated in the combination vaccine Tdap, which also contains protection against tetanus and diphtheria). It is important to understand that not all vaccines can be administered for this purpose. For example, live vaccines (such as varicella and MMR) should not be administered to those who are pregnant. Several other attenuated (inactivated) vaccines do not have data to support their use in those who are pregnant.

Monoclonal Antibody Vaccines

Monoclonocal antibody vaccines were also developed for use in infants. Nirsevimab (Beyfortus) is recommended for all infants younger than 8 months of age who are born during or who are entering their first RSV season. Infants younger than 8 months of age do not need nirsevimab if they were born 14 or more days after their mother received an RSV vaccine. Nirsevimab is also recommended for some children aged 8 through 19 months who are at increased risk for severe RSV disease and entering their second RSV season. Another monoclonal antibody can be used as prophylaxis treatment, palivizumab (Synagis) is used in those younger than 24 months of age with certain conditions that place them at increased risk for severe RSV disease. Palivizumab must be given once a month during RSV season.

Antibiotics

The term *antibiotics* refers to a large spectrum of medicines that are useful for treating and preventing infections caused by bacteria. These types of medications have no effect on viral, fungal, or other types of infections. Their improper use or use without proper indication can lead to resistance. This explains why antibiotics should not be

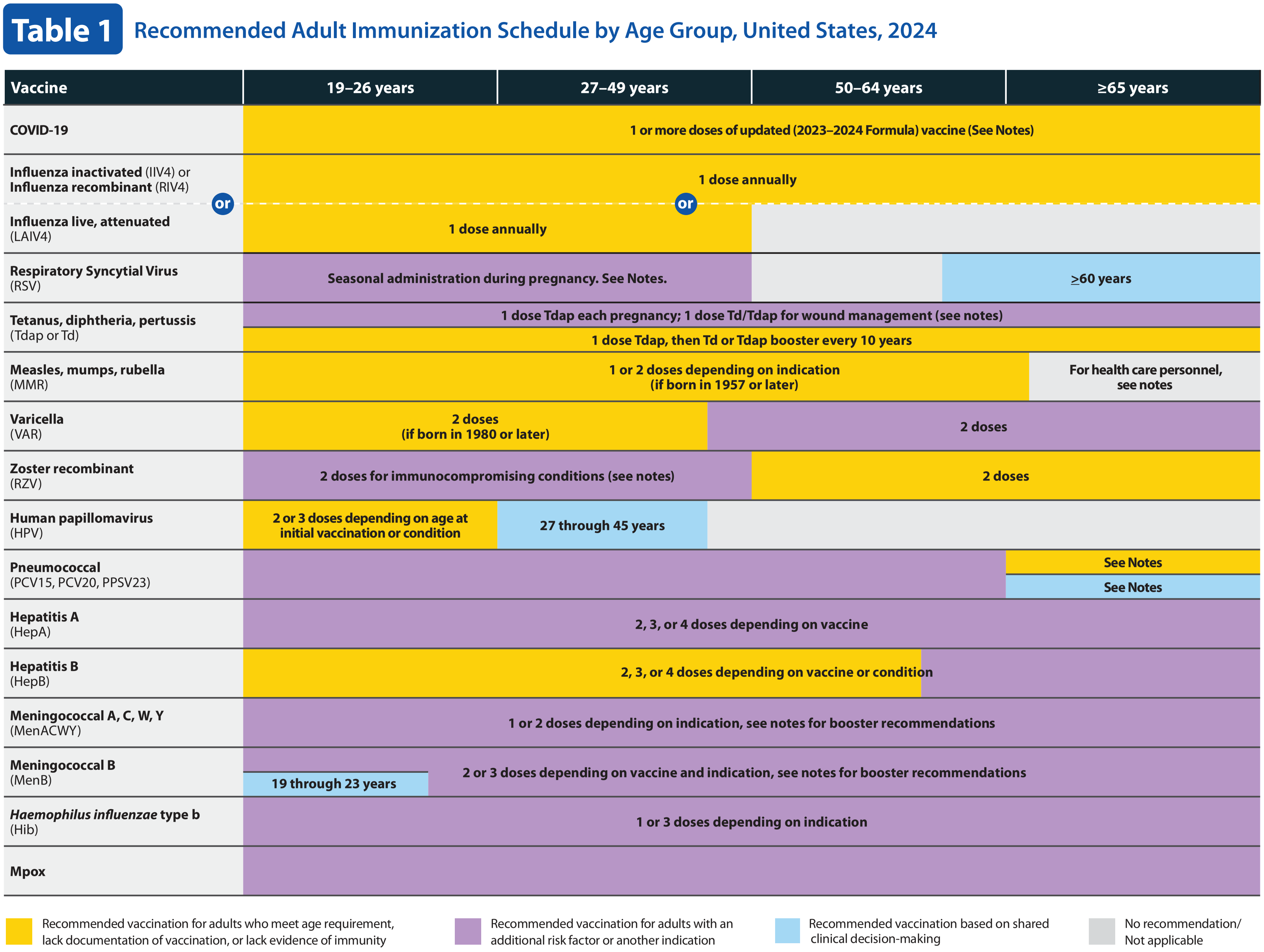


Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID-19	🟨 1 or more doses of updated (2023–2024 Formula) vaccine (See Notes)	🟨	🟨	🟨
Influenza inactivated (IIV4) or **Influenza recombinant** (RIV4) or	🟨 1 dose annually or	🟨 or	🟨	🟨
Influenza live, attenuated (LAIV4)	🟨 1 dose annually	🟨	⬜	⬜
Respiratory Syncytial Virus (RSV)	🟪 Seasonal administration during pregnancy. See Notes.	🟪	⬜ 🟦	🟦 ≥60 years
Tetanus, diphtheria, pertussis (Tdap or Td)	🟪 1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (see notes) 🟨 1 dose Tdap, then Td or Tdap booster every 10 years	🟪 🟨	🟪 🟨	🟪 🟨
Measles, mumps, rubella (MMR)	🟨 1 or 2 doses depending on indication (if born in 1957 or later)	🟨	🟨	⬜ For health care personnel, see notes
Varicella (VAR)	🟨 2 doses (if born in 1980 or later)	🟨 🟪	🟪 2 doses	🟪
Zoster recombinant (RZV)	🟪 2 doses for immunocompromising conditions (see notes)	🟪	🟨 2 doses	🟨
Human papillomavirus (HPV)	🟨 2 or 3 doses depending on age at initial vaccination or condition	🟦 27 through 45 years ⬜	⬜	⬜
Pneumococcal (PCV15, PCV20, PPSV23)	🟪	🟪	🟪	🟨 See Notes 🟦 See Notes
Hepatitis A (HepA)	🟪 2, 3, or 4 doses depending on vaccine	🟪	🟪	🟪
Hepatitis B (HepB)	🟨 2, 3, or 4 doses depending on vaccine or condition	🟨	🟨 🟪	🟪
Meningococcal A, C, W, Y (MenACWY)	🟪 1 or 2 doses depending on indication, see notes for booster recommendations	🟪	🟪	🟪
Meningococcal B (MenB)	🟪 2 or 3 doses depending on vaccine and indication, see notes for booster recommendations 🟦 19 through 23 years	🟪	🟪	🟪
***Haemophilus influenzae* type b** (Hib)	🟪 1 or 3 doses depending on indication	🟪	🟪	🟪
Mpox	🟪	🟪	🟪	🟪

🟨 Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of immunity

🟪 Recommended vaccination for adults with an additional risk factor or another indication

🟦 Recommended vaccination based on shared clinical decision-making

⬜ No recommendation/ Not applicable

Figure 25-3 2024 Adult Recommended Immunization Schedule.

Courtesy U.S. Department of Health and Human Services and the Centers for Disease Control and Prevention.

used for treatment of the common cold—because it is a viral infection. Organisms can also become resistant if infections are treated incompletely or for a shorter duration than prescribed. Bacterial infections can vary greatly; therefore, many different types of antibiotics have been developed and will be discussed in detail in the following section.

Clinical Connection

Antibiotic Duration of Therapy

Many different types of antibiotics are used in different scenarios to properly treat infection and to avoid resistance. Similarly, the duration of therapy can vary based on the type and severity of bacterial infection and should therefore be considered equally as important. Patients should be educated to take every antibiotic therapy regimen to completion, even if they begin to feel better or feel that they are completely better. This is important because each duration of therapy is designed by the prescriber to completely eliminate all harmful bacteria. If a treatment is stopped early, then only the weakest bacteria may have been eliminated, while the stronger (and possibly resistance-forming) bacteria are left to replicate. This can lead to a resistant superinfection or an infection that is more severe than the initial one that was being treated.

Aminoglycosides

Aminoglycosides, for example, gentamicin, possibly in combination with other antibiotics, are used to treat many infections. Examples of aminoglycosides include amikacin, gentamicin, and tobramycin. Because of poor absorption from the gastrointestinal (GI) tract, aminoglycosides are usually administered parenterally (i.e., IM or IV). The newest development in this class of antibiotics is plazomicin (Zemdri). Plazomicin is administered IV only and was developed to target multidrug-resistant Enterobacteriaceae. It has recently been approved to treat complicated urinary tract infections and pyelonephritis.

Serum levels (peak and trough) are often drawn to determine optimal dosing and lessen the risk of side effects. These levels measure the amount of drug in the blood at different times and are used to adjust subsequent doses and/or the frequency between doses. To avoid toxicity from decreased elimination, lower doses of aminoglycosides will be used in patients who have diminished renal function.

Serious side effects from aminoglycosides can include:

- ❗ *Nephrotoxicity*, generally reversible upon discontinuation
- ❗ *Ototoxicity*, both auditory (hearing loss) and vestibular (vertigo), may be permanent
- ❗ Neuromuscular blockade, including respiratory paralysis

Cautions or contraindications with aminoglycosides apply to:

Tinnitus, vertigo, and high-frequency hearing loss
Reduced renal function
Dehydration

Those who are pregnant or nursing

Infants or older adults

Interactions of aminoglycosides may occur with:

Other ototoxic drugs (e.g., amphotericin B, polymyxin B, bacitracin, and vancomycin)

General anesthetics or neuromuscular blocking agents (e.g., succinylcholine; can cause respiratory paralysis)

Antiemetics (may mask symptoms of ototoxicity)

Patient Education

Patients being treated with aminoglycosides should be instructed regarding:

Extreme importance of close medical supervision during therapy

Careful observation of intake and urinary output

Prompt reporting of any side effects, especially renal or hearing problems

Cephalosporins

Cephalosporins are related to penicillins, and *some* patients allergic to penicillin are also allergic to cephalosporins. In general, cephalosporins are broad-spectrum antibiotics active against many gram-positive and gram-negative bacteria. However, there are many different cephalosporins, and they vary widely in their activity against specific bacteria.

Cephalosporins are classified as first, second, third, fourth, or fifth generation, according to the organisms susceptible to their activity.

First-generation drugs, for example, cephalexin, are usually effective against gram-positive and some gram-negative organisms, such as those causing skin or soft tissue infections and UTIs. First-generation antibiotics are still commonly used for uncomplicated infections.

Second-generation drugs, for example, cefaclor and cefprozil, are usually effective against many gram-positive and gram-negative organisms, such as many strains causing bacterial pneumonia. Other second-generation cephalosporins include cefmetazole, cefotetan, and cefoxitin.

Third-generation drugs, for example, ceftriaxone, ceftazidime, cefdinir, cefpodoxime, cefoperazone, and cefixime, are usually effective against more gram-negative bacteria than the others and are sometimes used for the treatment of sexually transmitted infections (STIs) such as gonorrhea and in infections resistant to the first- and second-generation drugs. Notedly, ceftazidime is extremely active against *Pseudomonas aeruginosa.*

Cefepime (Maxipime), is the only fourth-generation drug, and is a parenteral cephalosporin with excellent activity against both gram-positive and gram-negative bacteria. It is considered a broad-spectrum antibiotic that can penetrate the cerebrospinal fluid. Although effective against both gram-positive and gram-negative bacteria, cefepime is not commonly used and is reserved for serious systemic infections that have a high likelihood of resistance.

Ceftaroline (Teflaro) is the only intravenous fifth-generation cephalosporin and is approved for the treatment of acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia. It is the first cephalosporin that is active against resistant gram-positive pathogens, including MRSA and vancomycin-resistant *S. aureus* (VRSA). Ceftaroline can also cover *Listeria monocytogenes* and *Enterococcus faecalis*.

Side effects of cephalosporins can include:

❗ Mild GI disturbances such as nausea, vomiting, and diarrhea

Cautions or contraindications with cephalosporins apply to:

Known allergies, especially to penicillin (3%–7% cross-sensitivity; more so with first-generation cephalosporins)

Prolonged use, possibly leading to superinfections or severe colitis (*Clostridium difficile*)

Interactions with cephalosporins can include:

Increased effectiveness with probenecid

Disulfiram-like reactions (flushing, tachycardia, shock) with alcohol ingestion and cefotetan

Patient Education

Patients being treated with cephalosporins should be instructed regarding:

Possible allergic reactions

Reporting any side effects to the physician

Taking the medication without regard to meals but with food if stomach upset occurs

Macrolides

Macrolides, such as erythromycin, clarithromycin, and azithromycin, are used for the treatment of many infections of the respiratory tract, for skin conditions such as acne, and for some STIs when the patient is allergic to penicillin. Macrolides are considered among the least toxic antibiotics and are therefore preferred for treating susceptible organisms under conditions in which more toxic antibiotics might be dangerous (e.g., in patients with renal disease, those who are pregnant, and infants).

In general, side effects of macrolides are minor, but special attention must be given to their interactions with other medications (refer to “Cautions or contraindications” with macrolides). Their most common use is experienced with uncomplicated upper respiratory infections, where azithromycin will be used for a 5-day regimen in the form of a Z-PAK (500 mg on the first day and then 250 mg for 4 days after) or a TRI-PAK (500 mg for 3 days). Clarithromycin, in combination with amoxicillin and lansoprazole (Prevpac Kit), is also used to treat *Helicobacter pylori* infection in patients with duodenal ulcer disease.

Side effects of a serious nature from macrolides are rare and mild side effects, usually dose related, can include:

- Nausea, vomiting, diarrhea, and cramps (take the medication with food or use smaller, more frequent doses)
- Urticaria and rash
- Superinfections

Cautions or contraindications with macrolides apply to patients with:

Liver dysfunction and GI disease

Electrolyte imbalances, certain cardiovascular diseases (can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm)

Interactions of macrolides (erythromycin and clarithromycin; potentially less with azithromycin) may occur with potentiation and possible toxicity of the following drugs:

Carbamazepine (Tegretol) (ataxia, dizziness, and drowsiness)
Cyclosporine (immunosuppressant with kidney or liver transplants)
Theophylline
Benzodiazepines (potentiation of sedative effects)
Warfarin (may prolong prothrombin time and bleeding)
Digoxin
Statins (lead to myopathy)

- **Warning:** Macrolides can cause abnormal, potentially fatal cardiac arrhythmias when combined with the following drugs:

  Calcium channel blockers—verapamil or diltiazem
  Antiarrhythmic agents (e.g., sotalol)
  “Azole” antifungals—fluconazole (Diflucan)
  Quinolones

Always check the label, or ask a pharmacist, for any other dangerous interactions with macrolides. Interactions vary depending on the specific drug.

Patient Education

Patients being treated with macrolides should be instructed regarding:

- Common GI side effects to expect
- Importance of reporting side effects for possible dosage adjustment or prescription of medication for symptomatic relief
- Taking medication with full glass of water 1 h before or 2 h after meals, unless stomach upset occurs (some forms can be taken without regard to meals)
- Not taking with interacting medications (refer to Interactions)

Penicillins

Penicillins are beta-lactam antibiotics produced from certain species of a fungus. They are used to treat many streptococcal and some staphylococcal and meningococcal infections, including respiratory and intestinal infections. Penicillin is the drug of choice for the treatment of syphilis and is also used prophylactically to prevent recurrences of rheumatic fever. Amoxicillin is the drug of choice for infective endocarditis prophylaxis in dental procedures (2 g orally 1 h prior to procedure) and is also used in combination with other drugs to treat *H. pylori* infection associated with *duodenal* ulcer disease. Amoxicillin is also considered first-line therapy for adolescents in the treatment of otitis media (ear infections).

Some semisynthetic penicillins, for example, piperacillin, have a wider spectrum of activity and are called extended-spectrum penicillins. These broad-spectrum penicillins are used in the treatment of infections caused by organisms such as *Pseudomonas.*

Some organisms, including both gram-positive and gram-negative bacteria, have become *resistant* to many forms of penicillin. To combat these organisms, amoxicillin is combined with clavulanic acid (Augmentin), and piperacillin with tazobactam (Zosyn), which are beta-lactamase inhibitors. They prevent beta-lactamase destruction of the penicillin with which they are combined, thus restoring or enhancing the intrinsic activity of the penicillin.

Serious side effects of penicillins can include:

- ❗ Hypersensitivity reactions ranging from rash to fatal anaphylaxis
- ❗ Superinfections (especially with oral ampicillin) and pseudomembranous colitis (*C. difficile*)
- ❗ Nausea, vomiting, and diarrhea

Cautions or contraindications with penicillins apply to patients with:

History of serious allergy to penicillins or other beta-lactams (e.g., anaphylaxis, hives) (anaphylaxis has been reported with parenteral, oral, or intradermal skin testing)

Treatment for severe reactions includes discontinuance of the drug, immediate administration of appropriate medications (e.g., epinephrine and corticosteroids), and maintenance of a patent airway. Administration of antihistamines with penicillin will *not* prevent hypersensitivity reactions.

Interactions of penicillins include:

Potentiation of penicillin with probenecid (may be desirable)

Potentiation with anti-inflammatory drugs such as methotrexate and salicylates given concomitantly (at the same time; monitor for increased side effects)

Antagonistic effect (delayed absorption) of oral penicillins when given with antacids or with food

Antagonistic effect of some other anti-infectives on penicillin

Penicillin V or ampicillin may inhibit the action of estrogen-containing oral contraceptives

Patient Education

Patients being treated with penicillins should be instructed regarding:

Discontinuing the medication and immediately reporting any hypersensitivity reactions (e.g., rash, swelling, or difficulty breathing)

Taking the medication on time as prescribed, for example, on empty stomach, 1 h before or 2 h after meals, with a full glass of water

Avoiding antacids and alcohol

Possible decreased effectiveness of estrogen-containing oral contraceptives

Carbapenems

Carbapenems such as meropenem (Merrem) belong to the beta-lactam class of antibiotics and have a very **broad spectrum** of activity against gram-negative and gram-positive organisms, including anaerobes and many multidrug-resistant pathogens. They are primarily used to treat pneumonia, febrile neutropenia, intra-abdominal infections, diabetic foot infections, and significant polymicrobial infections. A combination of meropenem and vaborbactam (Vabomere) is used to treat complicated urinary tract infections, including those that progress to kidney infection. Because of the potential for cross-reaction, carbapenems, similar to other beta-lactams, should be used cautiously in patients with documented penicillin allergies.

Refer to Table 25-1 for a summary of the aminoglycosides, cephalosporins, macrolides, penicillins, and carbapenems.

Table 25-1 Anti-Infective Agents: Aminoglycosides, Cephalosporins, Macrolides, Penicillins, and Carbapenems

Generic Name	Trade Name	Average Dosage
Aminoglycosides		
amikacin		IM, IV 10–15 mg/kg per day in one to three divided doses
gentamycin		IM, IV 3–6 mg/kg per day in one to three divided doses
tobramycin		IM, IV 3–6 mg/kg per day in one to three divided doses
plazomicin	Zemdri	IV 10–15mg/kg per day infused over 30 minutes
Cephalosporins (representative list only)		
First-Generation		
cephalexin	Keflex	PO cap, liquid, tab 250–500 mg q6h
cefazolin		IM, IV 250 mg q8h to 2 g q8h
Second-Generation		
cefaclor	Ceclor[a]	PO 250–500 mg q8h, cap, liq
cefuroxime	Ceftin	PO tab, liq 125–500 mg q12h
	Zinacef	IM, IV 750–1,500 mg q8h–q6h
Third-Generation		
cefdinir	Omnicef[a]	PO cap, susp 300 mg q12h or 600 mg q24h
cefotaxime	Claforan	IM, IV 1–2 g q8–12h
ceftazidime	Fortaz	IM, IV 1–2 g q8–12h
ceftriaxone	Rocephin	IV, deep IM 250 mg–2 g daily
Fourth-Generation		
cefepime	Maxipime	IV 500 mg–2 g q12h
		IM 500 mg–1 g q12h (UTI only)
Fifth-Generation		
ceftaroline	Teflaro	IV 600 mg q12h First cephalosporin to cover MRSA
Cephalosporin Combination Products		
ceftolozane/tazobactam	Zerbaxa	IV, 1.5 g q8h
ceftazidime/avibactam	Avycaz	IV, 2.5 g q8h
Macrolides		
azithromycin	Zithromax Z-Pak	PO tab, IR susp 500 mg on the first day, then 250 mg daily for 4 days
	Zithromax Tri-Pak	PO tab 500 mg daily three times
	Zmax	PO ER susp 2 g one time
	Zithromax	IV 500 mg daily

Generic Name	Trade Name	Average Dosage
clarithromycin	Biaxin	PO tab, liq 250–500 mg q12h
	Biaxin XL	PO ER tab 1,000 mg daily
erythromycin	Ery-Tab	PO tab, cap 250 mg q6h–500 mg q12h
	E.E.S., EryPed	PO tab, susp. 400–800 mg q6–12h
	Erythrocin	IV 15–20 mg/kg per day divided q6h
fidaxomicin	Dificid	PO tab 200 mg twice daily for 10 days
Penicillins		
amoxicillin	Amoxil	PO caps, liq 250 mg–1 g q8h; 875 mg q12h
		PO caps, liq 250–500 mg q6h
ampicillin		IM, IV 1–2 g q4–6h
dicloxacillin		PO, 125–500 mg q6h
penicillin G	Bicillin L-A	Deep IM 600,000–2.4 million units
penicillin VK	Pen VK	PO tab, liq 250–500 mg q6h
Extended-Spectrum		
amoxicillin-clavulanate	Augmentin	PO tab, liq 250–500 mg q8h, 875 mg q12h
	Augmentin ES	PO susp. 90 mg/kg in two divided doses (acute otitis media)
	Augmentin XR	PO tab 2,000 mg q12h
piperacillin-tazobactam	Zosyn	IV 2.25–4.5 g q6–8h
ampicillin-sulbactam	Unasyn	IV 1.5–3 g q6h
Carbapenems		
meropenem	Merrem	IV 500–1,000 mg q8h
meropenem/vaboractam	Vabomere	IV 4 g q8h

Note: Average dose ranges are listed. In severe infections, higher doses may be indicated. Many other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to the weight and condition of the child.

[a] This brand name is no longer marketed, but the name is still commonly used.

Quinolones

Quinolones, such as ciprofloxacin (Cipro), levofloxacin (Levaquin), and moxifloxacin (Avelox), are used in adults for the treatment of gonorrhea as well as some infections of the urinary tract, sinuses, lower respiratory tract, GI tract, skin, bones, and joints. Since these antibiotics are useful for treating many different infections, some organisms are showing increased resistance to the quinolones. Therefore, these agents should be reserved for infections (such as *Pseudomonas* infections) that require therapy with a fluoroquinolone or when a patient is allergic to other antibiotics. Newer quinolones, such as trovafloxacin, exhibit very strong activity against gram-positive bacteria and increased anaerobic coverage. Trovafloxacin is effective with a single daily dose, compared to older drugs in this class that require multiple doses per day.

Side effects of quinolones can include:

- ❗ Nausea, vomiting, diarrhea, abdominal pain, and colitis (especially older adult patients)
- ❗ Central nervous system (CNS) effects—headache, dizziness, confusion, irritability, seizures, and anxiety
- ❗ Superinfection (treat infection appropriately; may need to stop the drug)
- ❗ Phototoxicity (exposure to sunlight can cause severe sunburn)
- ❗ Possible cartilage or tendon damage (higher risk with older adults)

Cautions or contraindications with quinolones apply to:

Older adults, especially with GI disease or arteriosclerosis

Children or adolescents (*potential for cartilage damage*)

Those doing strenuous exercise during and several weeks after therapy (*potential for tendon rupture*)

Pregnancy and lactation

Seizure disorders

Cardiac disease (may cause or contribute to cardiac arrhythmias)

Interactions of quinolones may occur with:

Theophylline (ciprofloxacin can potentiate serious or fatal CNS effects, cardiac arrest, or respiratory failure)

probenecid (increased blood levels of Cipro)

Warfarin (increased risk of bleeding)

Antacids and other preparations containing Fe, Mg, Zn, Ca (decrease absorption; do not give within 2 h)

Sucralfate (Carafate) (contains aluminum ions, which decrease absorption)

Patient Education

Patients taking quinolones should be instructed regarding:

Not taking other medications without the physician's or pharmacist's approval

Drinking liberal quantities of fluids

Restricting caffeine intake—refer to CNS effects

Avoiding excessive exposure to the sun or use sunscreen with at least sun protection factor (SPF) 30

Avoiding strenuous exercise during and several weeks after therapy (potential for cartilage or tendon damage)

Reporting all side effects, especially rash or hypersensitivity signs

Older adult patients should follow preceding instructions, especially reporting GI effects or CNS effects (refer to side effects list)

Tetracyclines

Tetracyclines are broad-spectrum antibiotics used in the treatment of infections caused by rickettsia, chlamydia, or some *uncommon* bacteria. Diseases such as Rocky Mountain spotted fever, atypical pneumonia, some STIs, skin infections, and some severe cases of inflammatory acne are treated with tetracyclines. Doxycycline (Vibramycin) can also be used to treat skin and skin structure infections caused by community-acquired MRSA, as well as upper respiratory infections and Lyme disease. Three newer tetracyclines, eravacycline (Xerava), omadacycline (Nuzyra), and tigecycline (Tygacil), are also available and are designed to overcome tetracycline resistance.

Side effects of tetracyclines can include:

- ❗ Nausea, vomiting, and diarrhea (frequently dose related)
- ❗ Superinfections such as vaginitis and stomatitis
- ❗ Photosensitivity, with exaggerated sunburn

Cautions or contraindications with tetracyclines apply to:

Pregnancy and lactation
Children under age 8 years
Patients exposed to direct sunlight
Liver or GI disease

Interactions of tetracyclines may occur with the following antagonists (which decrease absorption):

Antacids, calcium supplements, and magnesium laxatives
Iron preparations and zinc
Antidiarrheal agents containing kaolin, pectin, or bismuth
Dairy products (doxycycline and minocycline not significantly affected)
Oral contraceptives (breakthrough bleeding or pregnancy may occur)

Tigecycline (Tygacil), a derivative of minocycline, is an IV antibiotic approved for the treatment of intra-abdominal and skin structure infections caused by several microorganisms, including MRSA; it also has significant activity against VRE. It should be reserved for more serious and resistant infections to maintain its full spectrum of activity.

Patient Education

Patients being treated with tetracyclines should be instructed regarding:

Avoiding exposure to sunlight
Avoiding this medication if pregnant or nursing, or if a child under 8 years of age
Administering preferably on an empty stomach with a full glass of water, 1 h before or 2 h after meals, unless there is gastric distress
Avoiding iron, calcium, magnesium, and antidiarrheal agents or dairy foods within 2 h of taking tetracyclines
Not taking at bedtime to prevent irritation from esophageal reflux
Discarding any expired drug—nephrotoxicity can result from taking outdated drug

Antifungals

Antifungal agents are used to treat specific susceptible fungal diseases. The medications are quite different in action and purpose, and are therefore treated separately.

Amphotericin B

Amphotericin B is administered IV for the treatment of severe systemic, potentially fatal infections caused by susceptible fungi, including *Candida.* It is sometimes considered the drug of choice to treat severe fungal infections resulting from immunosuppressive therapy (e.g., antineoplastic agents) or in patients with AIDS or those with severe illness (e.g., meningitis). *Severe side effects* are expected, and therefore close medical supervision (hospitalization) is usually required so that measures are available to provide symptomatic relief (e.g., antipyretics, antihistamines, and antiemetics). A newer antifungal, isavuconazole (Cresemba) is used for invasive aspergillosis or when amphotericin B is not able to be used in a patient.

Side effects of amphotericin B commonly include several of the following:

- ❗ Headache, chills, fever, hypotension, and tachypnea
- Infusion-related reactions
- ❗ Malaise, muscle and joint pain, and weakness
- ❗ Anorexia, nausea, vomiting, and cramps
- ❗ Nephrotoxicity (occurs to some degree in most patients; reversible in most cases upon completion of therapy)
- Anemia
- ❗ Hypokalemia and hypomagnesemia

Because of the many severe side effects and certain dose-limiting toxicities associated with conventional amphotericin B, other formulations have been developed. One example is a lipid-based product (Abelcet) that increases the tolerability of the drug without compromising its antifungal effects.

Fluconazole

Fluconazole (Diflucan) is one of the most widely prescribed antifungal agents. It acts against many fungal pathogens, including most *Candida,* without the serious toxicity of amphotericin B. Because of good patient tolerance and the convenience of both intravenous and oral dosage forms, this drug is appropriate for patients requiring prolonged antifungal therapy. It is used in the treatment of oropharyngeal (thrush) and esophageal candidiasis and serious systemic candidal infections (e.g., urinary tract and bloodstream infections). A single oral dose of fluconazole is effective in treating vaginal candidiasis, although it is now common practice to repeat the dose in 3–7 days to reduce the risk of recurrence or resistance. The newest antifungal used to treat vaginal candidiasis is ibrexafungerp (Brexafemme). In studies, ibrexafungerp showed increased success in reducing the risk of infection recurrence, but fluconazole eliminated infections faster.

Side effects of fluconazole can include:

- ❗ Moderate nausea, vomiting, abdominal pain, and diarrhea
- Rash

Cautions or contraindications with fluconazole apply to:

- Those who are pregnant or nursing
- Hepatic or renal disease

Interactions of fluconazole are common and may occur with:

- Warfarin (increased prothrombin time could cause hemorrhage)
- Oral antidiabetic agents (hypoglycemia can result)
- Rifampin (can lead to clinical failure of fluconazole)
- Statins (except pravastatin; increased risk of myopathy)
- Benzodiazepines (increased CNS effects)

Micafungin

Micafungin (Mycamine) belongs to one of the newer classes of antifungals and is administered via IV. Micafungin is indicated for the treatment of esophageal candidiasis and candidemia, and for stem cell transplantation prophylaxis. There are no major drug ***interactions*** with Mycamine.

Side effects of Mycamine can include:

- ❗ Infusion reactions
- ❗ Neutropenia

Cautions or contraindications with Mycamine apply to:

- Patients under age 18 years
- Pregnancy and breastfeeding
- Liver dysfunction
- Renal disease

Nystatin

Nystatin is structurally related to amphotericin B and is used orally to treat oral cavity candidiasis. It is also used as a fungicide in the topical treatment of skin and mucous membranes, for example, the diaper area, mouth, or vagina.

Side effects of nystatin are rare but may occasionally include nausea, vomiting, and diarrhea with high oral doses.

Caution should be taken in the use of nystatin with those who are pregnant or nursing.

There are no significant drug ***interactions*** with nystatin because of its lack of absorption from the gut.

Patient Education

Patients on antifungal therapy should be instructed regarding:

- Taking the medication for prolonged periods as prescribed, even after symptoms have subsided
- Reporting relapses promptly to the physician
- Reporting side effects immediately to the physician for possible dosage adjustment or symptomatic treatment
- Not taking any other medications at the same time without physician approval (refer to Interactions)

Antituberculosis Agents

Tuberculosis (TB) is caused by a bacterium called *Mycobacterium tuberculosis*, which primarily attacks the lungs. **Antituberculosis agents** are administered for two purposes: (1) to treat latent or asymptomatic infection (no evidence of clinical disease), for instance, after exposure to active tuberculosis and/or significantly positive PPD (purified protein derivative) skin test, and (2) to treat active clinical tuberculosis and prevent relapse.

For asymptomatic tuberculosis, the *treatment* consists of daily administration of isoniazid (INH) alone for 6–12 months to prevent development of the disease. For patients who are intolerant of INH or who are presumed to be infected with INH-resistant organisms, an alternative treatment of *rifampin with pyrazinamide* is given.

Treatment of clinical tuberculosis is challenging for two reasons:

1. Increasing incidence of tuberculosis is found particularly among certain high-risk populations (e.g., those with HIV, those with low levels of education and low incomes, racial or ethnic minorities, those who are homeless).
2. Organisms have become resistant (multidrug and extensive drug resistant) because of patient noncompliance or failure to complete the 6- to 24-month conventional treatment.

Therefore, the CDC recommends the following treatment regimen:

1. The American Thoracic Society (ATS) and the CDC currently recommend *short-course regimens* (i.e., at least 6 months) for the treatment of uncomplicated pulmonary tuberculosis in adults. According to the ATS, CDC, and American Academy of Pediatrics (AAP), short-course regimens are also suitable for children. Whenever possible to ensure compliance, *directly observed therapy (DOT)* should be used for all regimens administered two or three times per week.
2. The initial regimen for the treatment of tuberculosis should include INH given once daily for 2 months (in combination with rifampin, pyrazinamide, and ethambutol), followed by isoniazid and rifampin given daily, twice weekly, or 3 times per week for an additional 4 months (and at least 3 months beyond culture conversion). Patients who are HIV-positive should always receive induction therapy with four drugs by DOT. When drug susceptibility results are available, the regimen should be altered as appropriate. In addition, treatment may be extended to 9 months or longer in patients with HIV, dependent upon the clinical signs and symptoms or conversion of sputum cultures from positive to negative.

Although these drugs cross the placenta, they do not appear to have teratogenic effects. The CDC recommends that tuberculosis during pregnancy be treated initially with isoniazid, rifampin, and ethambutol for 9 months. Streptomycin is not included because it may cause congenital ototoxicity. Since recommendations change because of resistant strains and newly developed information, consulting www.cdc.gov/tb for current CDC recommendations is advised.

Side effects of *INH* and *rifampin* are usually more pronounced in the first few weeks of therapy and can be treated symptomatically. Pyridoxine (vitamin B_6) is often given (25–50 mg PO daily) with INH to reduce the risk of CNS effects and peripheral neuropathy. Dosage changes are sometimes required in cases of acute toxicity, but the medication must *not* be discontinued. Side effects can include:

❗ Nausea, vomiting, and diarrhea

❗ Hepatic toxicity (especially those over 35 years of age and children; refer to precautions)

❗ Body fluids colored red-orange with rifampin

Cautions or contraindications with INH and rifampin apply to:

Chronic liver disease or those with alcohol use disorder (periodic laboratory tests are required)

Impaired renal function

Interactions with rifampin include:

Antagonism by oral hypoglycemics, corticosteroids, digitalis, anticoagulants, and *estrogen* (serum levels of these drugs are reduced when taking rifampin)

Decrease in the serum concentration of antiretroviral protease inhibitors (PIs) (may result in HIV treatment failure)

Interactions with INH include:

Potentiation by phenytoin (Dilantin); increased action (possible toxicity) when taken with isoniazid

Increased risk of hepatotoxicity with rifampin (versus each agent alone)

Alcohol (increases the possibility of liver toxicity with both INH and rifampin)

Antacids (avoid 2 h before and after INH)

Side effects of ethambutol can include:

❗ Optic neuritis—with visual problems (reversible if discontinued early)

❗ Dermatitis, pruritus, headache, malaise, fever, confusion, joint pain, GI symptoms, and occasional peripheral neuritis

Cautions or contraindications with ethambutol include:

Visual testing before and during therapy

Impaired renal function (reduced doses indicated)

Diabetes, especially diabetic retinopathy

Ocular defects

Children under age 13 years—and only in children whose visual acuity can accurately be determined and monitored

Pregnancy—caution

Patients with gout (ethambutol can cause hyperuricemia)

Side effects of pyrazinamide can include:

- ❗ Hepatic toxicity
- Gout (increased uric acid)
- ❗ Hypersensitivity
- GI disturbances

Cautions or contraindications with pyrazinamide apply to:

- People with a history of gout
- Diabetes
- Severe hepatic disease or alcohol use disorder
- Children (potential toxicity)
- Those who are pregnant or nursing

Side effects of streptomycin, common to all aminoglycosides, include:

- ❗ Ototoxicity
- ❗ Nephrotoxicity

Streptomycin is administered by deep IM injection, alternating sites.

Patient Education

Patients taking antituberculosis agents should be instructed regarding:

- Taking rifampin on empty stomach for maximum absorption, or with food if nauseated
- Taking the prescribed medication for a *lengthy required period of time* even though asymptomatic
- Reporting side effects for possible dosage adjustment or prescription of other palliative medications to relieve discomfort
- Importance of frequent medical and laboratory checks
- Red-orange color of urine, feces, sputum, sweat, and tears with the use of rifampin
- Not wearing contact lenses during rifampin treatment
- Interactions with other drugs (e.g., *birth control pills may be ineffective*)
- Avoidance of alcohol
- Importance of visual testing periodically during ethambutol treatment

Refer to Table 25-2 for a summary of quinolones, tetracyclines, and antifungal and antituberculosis agents.

Table 25-2 Anti-Infective Agents: Quinolones, Tetracyclines, Antifungals, and Antituberculosis Agents

Generic Name	Trade Name	Average Dosage	Comments
Quinolones			
ciprofloxacin	Cipro	PO tab, susp 250–750 mg q12h; IV 200–400 mg q8–12h	Do C&S before Rx; cartilage or tendon damage possible; phototoxicity
	Cipro XR	PO tab 500–1,000 mg per day (UTIs only)	
levofloxacin	Levaquin	PO tab, soln, IV 250–750 mg q24h	

Generic Name	Trade Name	Average Dosage	Comments
moxifloxacin	Avelox	IV or PO 400 mg per day for 10–14 days	
trovafloxacin	Trovan	IV 300 mg q24h PO 200 mg q24h for 14 days	
Tetracyclines			
tetracycline		PO cap 250–500 mg q6–12h	Phototoxicity, discolored teeth in infants and children
doxycycline	Vibramycin	PO cap, tab, liq, IV 100–200 mg daily Can give double dose on day 1 as loading dose	Phototoxicity, discolored teeth in infants and children
tigecycline	Tygacil	IV 100 mg 1 time, 50 mg q12h	
minocycline	Minocin	PO 50–100 mg daily or bid	
eravacycline	Xerava	IV 1 mg/kg q12h for 10–14 days	
omadacycline	Nuzyra	IV 300–450 mg q24h infused over 30 minutes	
Antifungals			
amphotericin B	Abelcet, AmBisome	IV dose varies with the condition and product formulation	Special IV precautions; protect from light
fluconazole	Diflucan	PO, tab, susp, or IV 50–400 mg daily	Prolonged or maintenance doses frequently
micafungin	Mycamine	IV 100–150 mg daily	Protect from light
nystatin		PO tab, susp 500,000–1 million units 3 to 4 times per day, topical cream, oint, or powder	Continue treatment for 48 h after symptoms are resolved to prevent relapse
isavuconazole	Cresemba	IV, PO 372 mg q8h for 2 days, then 372 mg daily	Prodrug, each 372 mg dose contains 200 mg of the active isavuconazole
ibrexafungerp	Brexafemme	PO 300 mg q12h for 1 day	With or without food
Antituberculosis agents			
ethambutol	Myambutol	PO tab 15–25 mg/kg per day (max 1,600 mg)	Always with other medications
isoniazid	INH	PO tab, liq, IM 5 mg/kg per day (max 300 mg) or 15 mg/kg 3 times per week (up to 900 mg)	Preventive alone, or as treatment with other medications
pyrazinamide	PZA	PO tab 15–30 mg/kg per day (max 3 g) or 50–70 mg/kg 2 times per week	Always with other medications
rifampin	Rifadin	PO cap, IV 10 mg/kg per day (max 600 mg)	Initial phase with other drugs
streptomycin		IM (IV) 15 mg/kg per day (max 1 g)	Initial phase with other medications

Note: Other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to the weight and condition of the child.

Miscellaneous Anti-Infectives

Clindamycin

Clindamycin has a wider spectrum of activity than lincomycin, from which it is derived. It is used in the treatment of serious respiratory tract infections, septicemia, osteomyelitis, serious infections of the female pelvic area caused by susceptible bacteria, and *Pneumocystis jirovecii* pneumonia associated with AIDS (refer to AIDS section in this chapter). It is also used in prophylactic regimens in dental procedures for penicillin-allergic patients. Clindamycin may be a viable therapeutic option for community-acquired MRSA.

Side effects of clindamycin that frequently occur can include:

❗ Nausea, vomiting, diarrhea (drug should be discontinued if these symptoms develop), and colitis

Cautions or contraindications of clindamycin apply to:

History of GI, hepatic, or renal disease
Older adults
Children
Lactation (not recommended)

Metronidazole

Metronidazole (Flagyl) is one of the most effective drugs available against anaerobic bacterial infections (intra-abdominal, skin, gynecological, septicemic, bone or joint, lower respiratory tract). Metronidazole is also useful in treating Crohn's disease, antibiotic-associated diarrhea, rosacea, and *H. pylori* infection (in combination with other drugs to avoid the development of resistance). It is available in oral, parenteral, and topical formulations. Because of its mechanism of action, metronidazole is a highly effective antimicrobial. Resistance to metronidazole is very low.

Side effects of metronidazole include:

Anorexia, metallic taste, and xerostomia (dry mouth)
❗ Dark urine (common but harmless)

Cautions or contraindications with metronidazole apply to:

Lactation
CNS and hepatic diseases
Avoid alcohol during and 48 h after treatment (disulfuram-like reaction)

Clinical Connection

Disulfuram-Like Reactions

Disulfuram-like reactions occur when a drug contains a structural feature that inhibits the proper breakdown of alcohol in the body. This causes the build-up of acetaldehyde, which leads to severe "hangover" effects felt severely and immediately. These symptoms include flushing, nausea, vomiting, thirst, chest pain, vertigo, and hypotension. Flagyl (metronidazole) is a commonly prescribed anti-infective medication that produces such a reaction if taken with alcohol. Patients who are taking metronidazole should be counseled to avoid not only alcoholic beverages but also mouthwashes and elixirs that may contain alcohol. The medication Antabuse is prescribed to deter those recovering from alcohol use disorder from relapsing and using alcohol.

Vancomycin

Vancomycin is structurally unrelated to other available antibiotics. IV vancomycin is used in the treatment of potentially life-threatening infections caused by susceptible organisms. It is the drug of choice for MRSA, gram-positive infections in penicillin-allergic patients, and some infections of the heart valves (endocarditis).

Because vancomycin is poorly absorbed after oral administration, it is not used orally for widespread infections. It can be given orally to treat GI infections such as pseudomembranous colitis caused by the overgrowth of *C. difficile.* It is important to note that patients treated with IV vancomycin for systemic infections should not be switched to the oral form (a common practice with other antibiotics) because the oral form is not effective for treating systemic infections.

Side effects of vancomycin can include:

- ❗ Ototoxicity or nephrotoxicity (occurred primarily with older impure formulations) with IV use (discontinue with tinnitus, which may precede deafness)
- ❗ *Local effects* (give only IV with care; can cause necrosis or thrombophlebitis)
- ❗ Rash, anaphylaxis, and vascular collapse (hypersensitivity reactions reported in 5–10% of patients)

Cautions or contraindications with vancomycin apply to:

Older adults

Those who are deaf or hard of hearing

Renal impairment (serum drug levels are often drawn to determine the optimal dosing to maximize efficacy against MRSA; kidney function is also monitored frequently by serum creatinine and blood urea nitrogen [BUN] to determine dosage adjustments)

Pregnancy and lactation

Agents for VRE

Vancomycin has been used as “the last line of defense” against staphylococcal infections, as well as for certain streptococcal and enterococcal infections. However, in recent years, cases of VRSA and VRE have become more prevalent across the globe.

Linezolid (Zyvox) is indicated for gram-positive infections and is approved for the treatment of bacterial pneumonia, skin and skin structure infections, and MRSA and VRE infections, including those infections caused by susceptible organisms that are complicated by bacteremia. Linezolid is effective in treating diabetic foot infections, which are among the most serious complications of diabetes (leading to amputation in severe cases) and are the leading cause of diabetes-related hospitalizations.

Linezolid administered by IV infusion or orally has implications for medication safety and drug interactions. Inappropriate use, leading to an increase in resistant organisms, is a concern, and treatment alternatives should be carefully considered before using linezolid in outpatient settings.

Side effects of linezolid can include:

- ❗ Nausea, headache, and diarrhea (stop medication and contact the physician if blood is present in the stool or abdominal pain occurs)
- ❗ Anemia and thrombocytopenia

Cautions or contraindications with linezolid apply to:

- Cardiac disease and hypertension
- GI disease and hyperthyroidism
- Pregnancy and lactation
- Infants

Interactions of linezolid may occur with:

- Beta-blockers (worsen bradycardia)
- Antidepressants (e.g., selective serotonin reuptake inhibitors [SSRIs] can cause serotonin syndrome)
- Migraine medications (triptans)
- Sympathomimetics such as phenylephrine and pseudoephedrine (hypertensive reaction)
- Foods or beverages with high tyramine content

Daptomycin (Cubicin) is the first in a new class of antibiotics called lipopeptides with a spectrum of activity similar to vancomycin. It has greater activity against certain gram-positive bacteria. Daptomycin shows promise in treating VRE infections and endocarditis with associated bacteremia.

Side effects of daptomycin can include:

- Constipation, nausea, injection-site reactions, and headache
- ❗ Elevated levels of creatinine phosphokinase (CPK), leading to myopathy (monitor CPK levels weekly)

Cautions or contraindications with daptomycin apply to:

- Renal impairment (dosage adjustments required in severe disease)
- Pneumonia (daptomycin is inactivated by pulmonary surfactant and therefore is ineffective)

Refer to Table 25-3 for miscellaneous anti-infectives and agents for VRE.

Table 25-3 Miscellaneous Anti-Infectives and Agents for VRE

Generic Name	Trade Name	Average Dosage	Comments
Miscellaneous Anti-infectives			
clindamycin	Cleocin	PO cap, soln 150–450 mg q6h, peds 8–25 mg/kg per day divided doses, IM/IV 600 mg–2.7 g per day divided doses	
metronidazole	Flagyl	250–500 mg q8h–q6h IV, PO cap, tab (max 4 g per 24 h)	Take without regard to meals; avoid all forms of alcohol
	Flagyl ER	PO ER tab 750 mg per day for 7 days (for bacterial vaginosis)	Take on empty stomach
vancomycin	Vancocin	PO cap, soln 125–500 mg q6h for 7–10 days	For pseudomembranous colitis (IV route not effective)
		IV 10–20 mg/kg q12–24h	IV dose varies according to age, weight, indication, renal function, and serum drug monitoring
Agents for VRE			
daptomycin	Cubicin	IV 4–6 mg/kg q24h	Adjust dosage with severe renal impairment
linezolid	Zyvox	PO tab, susp, IV 600 mg q12h	Watch for interactions with psychiatric meds

Note: Other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to the weight and condition of the child.

Patient Education

Patients taking antibiotics should be instructed regarding:

- *Never* taking antibiotics for viral infections
- *Never* taking antibiotics that were left over from the treatment of a previous infection or ones that were prescribed for someone else
- Informing their physician *prior* to receiving any antibiotics of any allergies they have
- Informing their physician if they are pregnant or breastfeeding
- Unless directed otherwise, taking all antibiotics with a full glass of water on an empty stomach, at least 1 h before meals or 2 h after meals
- *Not* taking the medication with alcohol, antacids, or fruit juice
- If side effects occur, notifying the physician or pharmacist
- Reporting rash, swelling, or breathing difficulty to the physician *immediately*
- Taking antibiotics at prescribed times to maintain blood levels; if you miss a dose, do not double the next dose—resume with the next scheduled dose
- Taking the entire prescription *completely; not* discontinuing when the symptoms of infection disappear
- *Not* taking any other medications, prescriptions, or over-the-counter drugs at the same time as antibiotics without checking first with the physician or pharmacist regarding interactions

Sulfonamides

Sulfonamides are among the oldest anti-infectives. The increasing resistance of many bacteria has decreased the clinical usefulness of these agents. However, they are used most effectively in combination with other drugs, for example, with trimethoprim (sulfamethoxazole and trimethoprim).

Sulfamethoxazole and trimethoprim (Bactrim) is used for the treatment of UTIs, especially acute, complicated UTIs; enteritis (e.g., traveler's diarrhea); and otitis media. In higher doses, it may also be considered as an oral alternative to vancomycin when treating certain MRSA infections. Sulfamethoxazole and trimethoprim is used in the treatment and prevention of *P. jirovecii* pneumonia in patients with HIV (refer to the "Treatment of Human Immunodeficiency Virus/AIDS Infections" section in this chapter).

Side effects of sulfonamides include:

❗ Rash, pruritus, dermatitis, and photosensitivity

High fever, headache, stomatitis, and conjunctivitis

❗ Hepatic toxicity and renal damage

❗ Hypersensitivity reactions (can be fatal)

Cautions or contraindications with sulfonamides apply to:

Impaired hepatic function

Impaired renal function or urinary obstruction

Pregnancy or lactation

Interactions with sulfonamides include:

Potentiation of anticoagulants and oral antidiabetics

Antagonism of local anesthetics (e.g., procaine may inhibit the antibacterial action of sulfa)

Potentiation of phenytoin (Dilantin) (e.g., increasing serum drug concentrations)

Angiotension-converting enzyme (ACE) inhibitors, potassium salts, and potassium-sparing diuretics (hyperkalemia)

Patient Education

Patients taking sulfonamides should be instructed regarding:

Importance of drinking large amounts of fluid to prevent crystalluria (crystals in the urine)

Discontinuing sulfa at the first sign of rash

Reporting any side effects to the physician *immediately*

Avoiding exposure to sunlight

Ingesting sulfa with food, which delays but does not reduce the absorption of the drug

Urinary Anti-Infectives

A UTI, defined as a symptomatic inflammatory response from the presence of microorganisms in the urinary tract, is one of the most common bacterial infections for which patients seek treatment. First-line **urinary anti-infectives** for empiric treatment of uncomplicated lower UTI are sulfamethoxazole–trimethoprim (discussed earlier) and nitrofurantoin.

Nitrofurantoin (Macrobid and Macrodantin) is most commonly used for initial or recurrent UTIs caused by susceptible organisms. This medication is a recommended oral treatment option for cystitis (bladder infection) in females but not males because tissue concentrations are generally lower, resulting in inadequate treatment of occult prostatitis. Because of the achievement of lower tissue concentrations, nitrofurantoin is never used to treat pyelonephritis. Treatment must continue for an adequate period of time to be effective and minimize recurrence of infection.

Side effects of nitrofurantoin can include:

- ❗ Nausea and vomiting, which are less frequent if taken with milk or food
- ❗ Dark yellow or brown urine

Cautions or contraindications with nitrofurantoin apply to:

- Renal impairment (leads to loss of efficacy)
- Hepatic impairment
- Anemia
- Electrolyte abnormalities
- Asthma
- Pregnancy and lactation

Interactions of nitrofurantoin include:

- Probenecid (increased risk of nitrofurantoin toxicity)
- Antacids containing magnesium (decreased effectiveness)
- Quinolones (antagonistic to each other if both are used for UTI)

Patient Education

Patients taking nitrofurantoin should be instructed regarding:

- Importance of taking the medication for the required number of days
- Reporting side effects
- Taking medication with milk or food to reduce the incidence of nausea and vomiting
- Avoiding antacids
- Discoloration of the urine, which can stain underwear

Refer to Table 25-4 for a summary of the sulfonamides and urinary anti-infectives.

Table 25-4 Sulfonamides and Urinary Anti-Infectives

Generic Name	Trade Name	Dosage
Sulfonamides		
sulfamethoxazole (SMX) and trimethoprim (TMP)	Bactrim, Bactrim DS	Tab, suspension, IV 160 mg (TMP) q12h or 8–10 mg/kg per day in divided doses
Urinary Anti-infectives		
nitrofurantoin	Macrodantin, Furadantin	Cap, suspension 50–100 mg four times per day for 5–7 days
	Macrobid	Cap, 100 mg bid for 5–7 days
		Tab, soln 100 mg q12–24 h for 10–14 days

Note: Other anti-infective agents are used for UTI infections.

Antivirals

Acyclovir

The **antiviral agent** *acyclovir* is used predominantly in the treatment of herpes simplex, herpes zoster (shingles), and varicella zoster (chickenpox) infections. Acyclovir does not cure or prevent further occurrence of blister-like lesions. Topical application appears effective only with initial infections in relieving discomfort and shortening the healing time of lesions. Oral forms are most effective in the initial treatment of herpes to relieve pain and to speed healing of lesions and are also used to treat recurrent infections in some patients. In immunocompromised patients and children, parenteral treatment is recommended.

Herpes zoster (shingles) *is best treated within 24–72 h of onset* of rash (blister-like) or intense pain on the skin of one side of the trunk or head. Delayed treatment with an antiviral medication can lead to complications, such as intense pain and postherpetic neuralgia (PHN), lasting for weeks or months, especially in older adults. PHN is treated with tricyclic antidepressants (e.g., imipramine) or anticonvulsants (e.g., gabapentin).

Valacyclovir (Valtrex) is a prodrug that is converted to acyclovir as it is broken down within the body. The adverse reaction profile is the same as that for acyclovir, but improved bioavailability means less frequent dosing for valacyclovir. Famciclovir (Famvir) has a spectrum of activity that is similar to acyclovir but has a longer duration of action and can be dosed less frequently.

Side effects of acyclovir are not common but can include:

- ❗ Lethargy, tremors, confusion, and headache, especially with older adults
- ❗ Rash, urticaria, pruritus, and photosensitivity
- ❗ Nausea, vomiting, abdominal pain, and diarrhea

Cautions or contraindications with acyclovir apply to:

Children

Breastfeeding

Renal disease (adjust dosage)

Dehydration

Neurological abnormalities with high doses

Much work has been done to develop antiviral vaccines. Shingrix is an inactive vaccine administered intramuscularly for the prevention of shingles in persons aged 50 years and older. It is administered in a two-dose series, with the second dose being given 2–6 months after the first dose. It is superior to the former shingles vaccine (Zostavax), which is no longer commercially available. Shingrix is up to 97% effective at eliminating the risk of a shingles rash outbreak (compared to 50–70% for Zostavax). It can be administered at the same time as other vaccines (such as flu and pneumonia). Common side effects include local injection site reactions and fever, malaise, headache, and lethargy.

Patient Education

Patients being treated with acyclovir should be instructed regarding:

- The fact that acyclovir is usually effective only with *initial* infection in relieving pain and shortening healing of lesions but is *not* a cure, and there can be recurrences of lesions
- Reporting side effects
- Taking the medicine only as prescribed and not sharing the drug with others
- Finishing the full course as prescribed, even if feeling better
- Avoiding sexual intercourse when visible genital herpes lesions are present and using protection at other times

Antivirals for Acute Respiratory Infections

Oseltamivir (Tamiflu) and zanamivir (Relenza) belong to a class of antivirals called *neuraminidase inhibitors* and are indicated for the treatment of uncomplicated acute illness caused by influenza types A and B. Both are also indicated for prophylaxis but should not be considered a substitute for annual influenza virus vaccination, which remains the gold standard for reducing the impact of influenza. Instead, antiviral drugs are considered adjuncts to the prevention and control of influenza. Safety and efficacy for the prophylaxis of influenza infection in infants less than 1 year old (for Tamiflu) and children less than 7 years old (for Relenza) are not yet established. Oseltamivir is given orally and zanamivir via inhalation; both will shorten the duration of illness by about a day if taken *within 48 h of the onset of symptoms.*

Because zanamivir is given via inhalation, its main side effect is airway irritation and bronchospasm, especially in patients with asthma and chronic obstructive pulmonary disease (COPD). In patients who are susceptible to bronchospasm, a bronchodilator can be administered concurrently. Oseltamivir causes nausea, vomiting, and diarrhea in one out of four patients receiving it; these side effects can be lessened by taking the medication with food.

Baloxavir marboxil (Xofluza) is the newest medication for the treatment and prevention of influenza. It differs from Tamiflu and Relenza through its mechanism of action, which inhibits viral RNA synthesis. It is used in the same manner as other anti-influenza medications and has a side effect profile similar to that of Tamiflu.

Recently, the FDA has authorized or approved several antiviral medications used to treat mild to moderate COVID-19 in people who are more likely to get very sick. These antiviral treatments target specific parts of the virus to stop it from multiplying in the body, helping to prevent severe illness and death. Several options are available by prescription for treating COVID-19, and like those antivirals used for influenza, they should be started as soon as possible after symptoms begin or diagnosis occurs. The antiviral options are nirmatrelvir with ritonavir (Paxlovid), remdesivir (Veklury), and molnupiravir (Lagevrio).

Ribavirin

A drug with the broadest spectrum of antiviral activity, *ribavirin* is used via nasal and oral inhalation for the treatment of infants and young children with respiratory syncytial virus (RSV) infections. It has also been used orally and parenterally (IV form available only through the CDC) in the treatment of other severe viral infections in adults, for example, Lassa fever, hantavirus, and hepatitis C (in combination with interferon alfa).

Side effects of ribavirin can include:

Respiratory complications
Hypotension and cardiac arrest

Contraindicated during pregnancy or lactation. Health care professionals and visitors who are pregnant or lactating should be warned about the *serious risk of close contact with patients receiving ribavirin inhalation therapy.*

Interactions of ribavirin with nucleoside reverse transcriptase inhibitors (NRTIs; agents for HIV), depending on the specific agent, can:

Antagonize antiviral action against HIV
Cause lactic acidosis
Cause hepatic failure

Refer to Table 25-5 for a summary of the antiviral agents.

Table 25-5 Antivirals

Generic Name	Trade Name	Dosage
Antivirals		Take entire Rx even if feeling better
For Herpes Infections		
acyclovir	Zovirax	PO tab, cap, susp 200–800 mg five times per day q4h, IV 5–10 mg/kg q8h
famciclovir	Famvir	PO tab 500 mg q8h
valacyclovir	Valtrex	PO tab 1,000 mg q8h
zoster vaccine	Zostavax	0.65 mL SC one time for prevention
For Influenza		
baloxavir marboxil	Xofluza	PO 40–80 mg as a single dose Same dose for treatment and prophylaxis
oseltamivir	Tamiflu	PO cap, susp 75 mg bid for 5 days
zanamivir	Relenza Diskhaler	Inhale 10 mg q12h for 5 days

Generic Name	Trade Name	Dosage
For COVID-19		
nirmatrelvir/ritonavir	Paxlovid	PO 300/100 mg q12h for 5 days Must begin within 5 days of when symptoms start
remdesivir	Veklury	IV dosing based on weight for 3 days Must begin within 7 days of when symptoms start
molnupiravir	Lagevrio	PO 800 mg q12h for 5 days Must begin within 5 days of when symptoms start
For RSV		
ribavirin	Virazole	Powder/sol—inhalation
	Various	Oral, dose varies; primarily for hepatitis C

Treatment of Human Immunodeficiency Virus/AIDS Infections

Treatment of HIV and AIDS infections is a highly specialized field. Those actively practicing in that field must be updated frequently on the many *new* medications and *frequently changing protocols*. If you are not actively practicing in this area, you would not be expected to be familiar with all of the many drugs for HIV (refer to Table 25-6). However, all health care professionals should be aware that there are numerous side effects and interactions specific to individualized medications.

Table 25-6 Drugs for HIV/AIDS

Generic Name	Trade Name	Class Adverse Effects
Antiretrovirals[a]		
Protease Inhibitors (PIs)		
atazanavir	Reyataz	GI intolerance, hyperglycemia, dyslipidemia, many drug interactions
darunavir	Prezista	
lopinavir/ritonavir	Kaletra	
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs)[b]		
abacavir	Ziagen	Lactic acidosis, liver dysfunction
lamivudine/zidovudine	Combivir	
tenofovir/emtricitabine	Truvada	
	Descovy	

(*Continued*)

Table 25-6 Drugs for HIV/AIDS (*Continued*)

Generic Name	Trade Name	Class Adverse Effects
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
efavirenz	Sustiva	Rash, hepatotoxicity, many drug interactions
rilpivirine	Edurant	
Fusion Inhibitors (FIs)		
enfuvirtide	Fuzeon	Injection site reactions
CCR5 Antagonists		
maraviroc	Selzentry	Hepatotoxicity
Integrase Inhibitor		
raltegravir	Isentress	GI intolerance, CNS effects

[a] Other drugs and combinations are being used investigationally in the treatment of HIV- and AIDS-related diseases. Dosage varies with condition. *Check dosage very carefully.*

[b] *Other combination products available in this class are not listed.*

The treatment of patients with HIV is complex because of the availability of numerous **antiretroviral (ARV) agents** and the rapid growth of new information. A patient's clinical condition, readiness for lifelong therapy, CD4 count, and plasma viral load are essential parameters to be used in decisions to initiate or change therapies. Once patients with HIV experience immunosuppression based on decreases in CD4 counts, they are at risk for many **opportunistic infections**. Current guidelines for the initial treatment of HIV infection recommend the use of two NRTIs with a protease inhibitor, a fusion inhibitor, or a non-nucleoside reverse transcriptase inhibitor (NNRTI). Consult https://clinicalinfo.hiv.gov/en/guidelines for the most current treatment information.

Prevention of HIV is an important use for ARV agents. PrEP (pre-exposure prophylaxis), when taken as prescribed, is highly effective for preventing HIV, even if exposure occurs. PrEP is recommended for people who may be exposed to HIV via sex or drug use. There are two pills approved for use as PrEP: Truvada and Descovy. These drugs are taken each day. PEP (post-exposure prophylaxis), when taken within 72 h of suspected or known exposure to HIV, reduces the risk of getting HIV by more than 80%. PEP is a combination of 3 drugs taken once or twice a day for 28 days. The CDC recommends tenofovir, emtricitabine, and either raltegravir or dolutegravir.

Antiretroviral Protease Inhibitors

Protease inhibitors (PIs) block the activity of the HIV enzyme essential for viral replication late in the viral life cycle. The first PI to be approved was saquinavir (Invirase), followed by more than eight other ARV protease inhibitors (refer to Table 25-6 for names of other PIs).

Side effects can include:

All PIs are associated with GI intolerance, including nausea, vomiting, and diarrhea

Taste alteration in patients receiving ritonavir, especially the liquid formulation

Fat redistribution, hyperlipidemia, and insulin resistance

Hyperglycemia, new-onset diabetes mellitus, diabetic ketoacidosis, and exacerbation of existing diabetes

Increased spontaneous bleeding episodes in hemophilia patients (joints, soft tissues, intracranial, and GI)

Indinavir may cause kidney stones (patients should drink at least 1.5 L per day of water to ensure adequate hydration and prevent kidney stones)

Interactions with PIs are many. Certain "statin" drugs are either contraindicated or require lower doses when given with PIs because of an increased risk of myopathy. Check with the pharmacist before administering PIs with other drugs.

Dietary considerations with PIs:

Most PIs should be taken with food to reduce nausea and gastric irritation.

Always check instructions regarding administration.

Patient Education

Patients taking antiretrovirals should be instructed regarding:

The fact that there is no cure for HIV, and opportunistic infections may develop

Taking the drug in an upright position with full glass of water

Taking the drug exactly as prescribed and not stopping abruptly

Taking into account dietary considerations

Reporting any change in health status or side effects

Not exceeding the prescribed dosage

Not sharing the drug with others

Not taking any other drugs unless prescribed

Nucleoside Reverse Transcriptase Inhibitors

NRTIs inhibit an enzyme responsible for viral replication early in the viral life cycle. Zidovudine (ZDV, Retrovir) was the first agent to be approved for the treatment of HIV, followed by more than six other NRTIs (refer to Table 25-6 for names of other NRTIs).

Because of the development of resistance, NRTIs must be used in combination with other ARVs. Combivir, a combination of zidovudine and lamivudine (there are currently six other combinations), allows patients to reduce the number of pills needed, which can be upward of 20 a day for certain drug combinations. Combivir plus Kaletra is a preferred regimen in pregnancy. Most NRTIs are dose adjusted in patients with renal dysfunction.

Side effects of NRTIs can include:

Lactic acidosis and liver dysfunction (infrequently, but with a high mortality rate)

Flare-up of chronic active hepatitis B with abrupt withdrawal of emtricitabine and lamivudine

Bone marrow suppression consisting of anemia and/or neutropenia with zidovudine

Pancreatitis with didanosine

Peripheral neuropathy and pancreatitis with didanosine and stavudine

Abacavir has been associated with hypersensitivity reactions that can be fatal. Prior to starting abacavir, it is recommended to obtain an HLA B5701 genetic test. If positive, abacavir should not be started because the patient will be at a higher risk of developing a life-threatening hypersensitivity reaction.

Interactions of NRTIs include:

Alcohol

Antacids and iron preparations

Other drugs that are nephrotoxic

Non-Nucleoside Reverse Transcriptase Inhibitors

NNRTIs also inhibit an enzyme responsible for viral replication early in the viral life cycle. Nevirapine (Viramune) was the first NNRTI to be approved, followed by four others (refer to Table 25-6 for names of other NNRTIs). NNRTIs must be administered in combination with other ARVs due to development of resistance.

Adverse reactions with NNRTIs can include:

Hepatotoxicity and cutaneous reactions

Psychiatric effects with efavirenz and rilpivirine

Side effects of NNRTIs can include:

CNS symptoms, including dizziness, insomnia, abnormal dreams, and confusion

Interactions with NNRTIs are many. Check with a pharmacist before administering with other drugs.

Dietary considerations with NNRTIs:

Always check instructions regarding administration, as some should be given ac and some pc.

Fusion Inhibitors

The class of ARV agents called fusion inhibitors (FIs) has been shown to block entry of HIV into cells, which may keep the virus from reproducing. Enfuvirtide (Fuzeon) was the first FI approved for treatment-experienced patients with ongoing HIV replication despite current ARV use. It is administered by subcutaneous injection twice daily.

Almost all patients develop local site reactions to enfuvirtide, usually consisting of mild or moderate pain, erythema, itching, induration, nodules, and cysts. It is important to remember to rotate injection sites.

CCR5 Antagonists

CCR5 antagonists block a coreceptor required for HIV entry into human cells. Maraviroc (Selzentry) is the first oral CCR5 antagonist and is used in conjunction with other ARVs. Hepatotoxicity has been reported and may be accompanied by signs or symptoms of a systemic allergic reaction. Do not use maraviroc with St.

John's wort, as this combination can lead to treatment failure, and avoid certain ARV combinations.

Integrase Inhibitor

Raltegravir (Isentress) is the first ARV in this class that is designed to slow the advancement of HIV infection by blocking the enzyme needed for viral replication. It is indicated for use in combination with other ARVs in treatment-experienced adults. Most common adverse effects are nausea, headache, diarrhea, and pyrexia. Rifampin can decrease plasma concentrations of raltegravir. Use caution with certain ARV combinations.

In summary, note that many other anti-infective agents in all of the categories discussed in this chapter are available. This is a representative sample of drugs most commonly in use along with their indications, precautions or contraindications, side effects, and cautions.

Case Study A

Anti-Infective Drugs

A patient suffered a torn Achilles tendon while playing flag football with their friends. The patient underwent an Achilles tendon repair, and 10 days postoperatively, they noticed swelling, redness, and warmth around the incision and yellow discharge seeping from it.

1. The prescriber would use what to determine the appropriate antibiotic therapy?
  a. culture and sensitivity test
  b. serum creatinine test
  c. empiric evidence test
  d. CBC with differential test

2. If the patient requires aminoglycosides, why are these most often administered either by IV or IM injection?
  a. Medications cause GI distress when given orally.
  b. A therapeutic dose cannot be reached when administered orally.
  c. Pills are difficult for the patient to swallow.
  d. The medication is poorly absorbed from the GI tract.

3. What method is used to determine optimal dosing for the aminoglycoside (gentamycin)?
  a. repeat C&S of wound drainage
  b. serum peak and trough levels
  c. 24-h urine analysis
  d. CBC with differential

4. The patient was prescribed gentamycin. What side effect can gentamycin IV cause?
  a. syncope
  b. nephrotoxicity
  c. polyuria
  d. lower extremity cramping

5. The patient is taken back to the operating room (OR) for a wound debridement, and gentamycin is ordered again for their wound infection. Postoperatively, an interaction may occur between gentamycin and which category of drug?
  a. antiemetics
  b. anti-inflammatories
  c. analgesics
  d. muscle relaxants

Case Study B

UTI Infection

A patient is diagnosed with a UTI after complaining of burning upon urination. The physician is preparing to write a prescription for nitrofurantoin.

1. Prior to prescribing nitrofurantoin, the physician reviews the patient's medical history because this medication should be used with caution in patients with
- a. diabetes
- b. renal impairment
- c. hypertension
- d. COPD

2. A common side effect of nitrofurantoin is
- a. tinnitus
- b. numbness of hands
- c. abdominal pain
- d. brown-colored urine

3. The physician reviews the patient's current medications because nitrofurantoin can interact with a certain drug that decreases its effectiveness. Which drug is this?
- a. probenecid
- b. warfarin
- c. an antacid containing magnesium
- d. ibuprofen

4. Which of the following should the nurse make sure to include in the patient's instructions for nitrofurantoin?
- a. Urine may become discolored.
- b. Take the medication with an antacid.
- c. Stop taking the medication when symptoms disappear.
- d. Take the medication with water.

5. The duration of drug therapy using nitrofurantoin for a UTI is how many days?
- a. 3
- b. 7
- c. 10
- d. 14

Chapter Review Quiz

Match the medication in the first column with the condition in the second column that it treats. Conditions may be used more than once.

Medication	Condition
1. _______ nitrofurantoin (Macrodantin)	**a.** Herpes zoster and herpes simplex
2. _______ nystatin	**b.** MRSA and VRE
3. _______ fluconazole (Diflucan)	**c.** Urinary tract infections
4. _______ linezolid (Zyvox)	**d.** Tuberculosis
5. _______ ethambutol	**e.** Acne
6. _______ valacyclovir	**f.** Fungus
7. _______ erythromycin	**g.** Influenza A

Choose the correct answer

8. What is the best method for preventing the spread of infection?

a. Bleach patient care areas daily.
b. Have patients wear a mask.
c. Observe routine handwashing.
d. Require masks and gloves for all health care personnel.

9. An over-response of the body to a specific substance is called

a. hyperimmunity
b. superinfection
c. direct toxicity
d. allergic hypersensitivity

10. A sudden onset of dyspnea, chest congestion, shock, and collapse is called

a. anaphylaxis
b. nephrotoxicity
c. dyscrasia
d. prophylaxis

11. When administering an anti-infective drug to an older patient, which of the following may be indicated for safe treatment?

a. more frequent dosing
b. an increased dose
c. a lower dose
d. once-a-day dosing

12. The best treatment for herpes zoster (shingles) will start within how many hours of the onset of the blister-like rash?

a. 24
b. 24–72
c. 48
d. 96

13. The physician orders an antibiotic to be given to a patient before surgery. What is this type of dosing called?

a. antiseptic
b. predetermined
c. prophylactic
d. proactive

14. Caution needs to be exercised when prescribing a cephalosporin to a patient with which known allergy?

a. seafood
b. penicillin
c. latex
d. peanuts

15. Which medication category may cause discolored teeth in young children?

a. tetracyclines
b. cephalosporins
c. aminoglycosides
d. carbapenems

16. What medication is used to treat oral cavity candidiasis?

a. nystatin
b. rifampin
c. isoniazid
d. amphotericin B

17. A patient receiving zanamivir might experience which side effect?

a. phlebitis
b. airway irritation
c. nausea
d. rash

18. The drug of choice for treating methicillin-resistant *Staphylococcus aureus* is

a. metronidazole
b. ciprofloxacin.
c. vancomycin
d. doxycycline

19. A patient taking an antiretroviral should be instructed that

a. OTC drugs are permitted in conjunction with an antiretroviral as long as dosing instructions on the antiretroviral's label are followed
b. the drug should be taken in an upright position with a full glass of water
c. the drug reduces the risk of HIV transmission to other individuals
d. the medication may be stopped abruptly

20. What side effect might protease inhibitors cause?

a. exacerbation of existing diabetes
b. constipation
c. dehydration
d. urinary tract infection

21. The single best way to reduce the spread of the influenza virus is what?

a. the annual flu vaccine
b. mask wearing and physical distancing
c. handwashing
d. avoiding public transportation

22. Antibiotic-resistant bacteria can form as a result of all of the following EXCEPT

a. taking an antibiotic for a shorter duration than prescribed
b. overprescribing of an antibiotic or antibiotic class
c. using an antibiotic for an incorrect infection
d. using a combination of antibiotics rather than a single antibiotic

23. Which of the following is NOT used in the prevention or treatment of respiratory syncytial virus (RSV)?

a. Abrysvo
b. Beyfortus
c. Ribavirin
d. Paxlovid

24. Which vaccine is NOT administered to pregnant persons with the intention of passing antibodies to an unborn fetus?

a. Tdap (whooping cough)
b. Varicella (chickenpox)
c. Abrysvo (RSV)
d. None of the above are administered for this purpose

25. The best preventive action a person can take to avoid the shingles rash is

a. receiving one dose of Shingrix
b. receiving two doses of Shingrix
c. prophylactically taking acyclovir 400 mg daily
d. increasing exercise and improving the diet

Chapter 26

Antineoplastic Drugs

Key Terms and Concepts

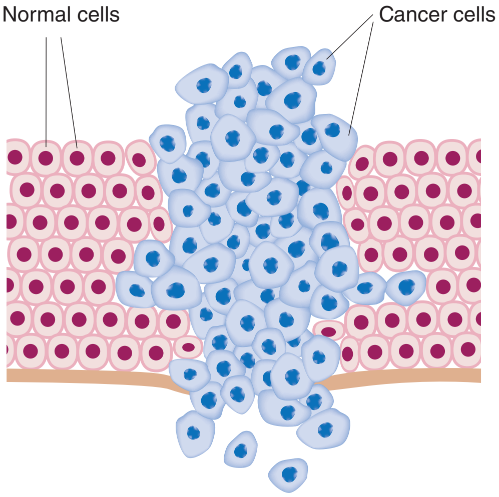
Antineoplastic
Benign
Chemotherapy
Cytotoxic
Dose-limiting side effects
Immunosuppressive
Malignant
Palliative
Proliferating

Objectives

Upon completion of this chapter, the learner should be able to:

1. Describe the major groups of antineoplastic agents and their side effects.
2. Describe appropriate interventions in caring for patients receiving antineoplastic agents.
3. Explain precautions in caring for those receiving radioactive isotopes.
4. Describe the responsibilities of those caring for patients receiving chemotherapy.
5. Explain appropriate education for the patient and family when antineoplastic agents are administered.
6. List safety factors for those who care for patients receiving cytotoxic drugs.

A healthy body needs cells to reproduce and grow in an orderly, regulated manner. However, sometimes conditions in the body are altered, and this triggers abnormal changes in the way the cells reproduce and grow. These triggers can cause cell growth to become uncontrolled, leading to overproduction or disorganized or impaired cellular development (Figure 26-1).



Ailia Medical Media/Shutterstock.com.

Figure 26-1 Cancer cells are identified by uncontrolled cell growth.

This unregulated growth can lead to abnormal cell, tissue, and tumor development. Tumors can be classified as either **benign** (noncancerous) or **malignant** (cancerous). In general, benign tumors are less dangerous than malignant tumors. Benign tumors are usually removed because their size is causing pain, inflammation, or complications to other body systems. Malignant tumors are removed for many reasons, but most importantly to reduce the chance of the cancerous cells spreading to other parts of the body.

Antineoplastic (against new tissue formation) refers to an agent that counteracts the development, growth, or spread of malignant cells and is therefore used to treat various types of cancers. Cancer therapy frequently includes a combination of surgery, radiation, and chemotherapy.

Chemotherapy is a constantly growing field in which many old and new drugs and drug combinations are used for **palliative** (alleviation of symptoms) effects or for long-term or complete remission in the early treatment of cancer. Antineoplastic drugs are **cytotoxic** (destructive to cells), especially to cells that are **proliferating** (reproducing rapidly). Unfortunately, the toxic effects of the antineoplastic drugs are not confined to malignant cells alone; they also affect other proliferating tissues, such as the bone marrow, gastrointestinal (GI) epithelium, skin, hair follicles, white blood cells (WBCs), and epithelium of the gonads, resulting in numerous adverse side effects. It should be noted that all of these “normal” cell tissues affected by chemotherapy are ones that naturally grow and proliferate at a higher rate than other cells found in the body.

Significant developments continue in the use of targeted therapies that are designed to target only cancer cells, thereby sparing normal tissues. This therapy reduces host toxicity while simultaneously increasing toxicity to cancer cells and improving survival rates in patients with cancer. Many new drugs in the targeted therapy category called signal transduction inhibitors (STIs) are given by the *oral route*. The first cancer *treatment* vaccine for certain males with metastatic prostate cancer was recently approved, and many others are being tested in clinical trials.

Personalized oncology medicine, utilizing pharmacogenomic biomarkers, is a developing field in which, based on their genetic profile, individual patients and individual cancers that respond differently to oncology medications can be identified. This is the basis for the first-line treatment of metastatic breast cancer in patients with tumors that produce excess amounts of a protein called HER2, discussed later in this chapter.

Many antineoplastic agents also possess **immunosuppressive** properties; that is, they may decrease the production of WBCs and antibodies and reduce the inflammatory reaction. Suppression of the immune response results in the patient’s increased susceptibility to infection.

Antineoplastic drugs are frequently administered in high doses on an *intermittent* schedule. Most normal tissues have a greater capacity for repair than do most malignant tissues, and therefore normal cells may recover during the drug-free period.

Chemotherapy is *individualized* and frequently modified according to the patient’s response to the treatment. A *combination of several drugs* is frequently prescribed to delay the emergence of resistance, with the choice of agents based on the type of malignancy, areas involved, extent of the cancer, physical condition of the patient, and other factors. Careful planning is required to maximize the effectiveness of therapy and to minimize the side effects and discomfort for the patient. Treatment strategies are often determined based on the aggressiveness of the cancer cells and how far the cancer has progressed upon diagnosis. Understanding the treatment program and possible side effects is essential for all concerned: the health care professional, the patient, and the family. Preplanning includes provision for symptomatic relief, such as antiemetics (drugs to prevent nausea), as well as reassurance and the availability of support staff to answer questions, explore feelings, and allay fears.

The treatment of cancer is highly complex. Only health care professionals in oncology units, cancer treatment centers, and oncologist's offices would be expected to know the names of the numerous drugs. However, anyone who is in contact with patients on antineoplastic therapy should be aware of the frequent possible side effects and appropriate interventions for the comfort of the patient. Patient education and support are extremely important.

Antineoplastic agents can be generally classified into nine major groups: (1) antimetabolites; (2) alkylating agents; (3) mitotic inhibitors (plant alkaloids, taxanes); (4) antitumor antibiotics; (5) hormones and hormone modifiers (corticosteroids, antiestrogens, and antiandrogens); (6) biological therapies (interferons, colony-stimulating factors [CSFs], and monoclonal antibodies [MABs]); (7) targeted cancer therapies (STIs); (8) vaccines; and (9) radioactive isotopes.

Refer to Table 26-1 for a summary of antineoplastic agents and representative drugs for each class.

Table 26-1 Antineoplastic Agents

Drug Class	Representative Drug	Comments
Antimetabolites	methotrexate	Also used for psoriasis, rheumatoid arthritis, and lupus. Weekly Dosing (not daily)
Alkylating agents	cisplatin	Can lead to leukemia after treatment concludes
Mitotic inhibitors	vinorelbine	Also called plant alkaloids, taxanes For IV use only, fatal if given intrathecally
Antitumor antibiotics	doxorubicin	Are used for a wide variety of cancers, but lifetime dosing limits their long-term use. Cardiotoxicity can occur with extended use.
Hormones and hormone modifiers	tamoxifen	This drug class includes corticosteroids, antiestrogens, and antiandrogens
Biological therapies	bevacizumab	Biologic therapies can be used to fight cancer cells (interferon, monoclonal antibodies) or to help combat side effects (Epogen, Procrit)
Signal Transduction Inhibitors	imatinib	Also called targeted cancer therapies, these drugs target a specific component of proliferation based on cancer type.
Radioactive isotopes	radioactive iodine	Newest therapies couple monoclonal antibodies with radioactive isotopes.

About half of all cancer patients receive some type of radiation oncology therapy sometime during the course of their treatment. Radioactive substances are placed close to or implanted in the cancerous tissues (internal radiation therapy), or an external-beam radiation is passed in three dimensions, which is made possible with computer technology.

Only one or two examples of medications are presented for each category to identify the side effects specific to that group. It is not necessary to remember the names of these drugs, as they are only representative of the many antineoplastic agents available. However, if you work extensively with cancer patients, knowing the drug names is important, and the National Cancer Institute website can provide you with all the latest drugs and treatments available for the various types of cancers.

Antimetabolites

Antimetabolites work by interfering with DNA synthesis, repair, and cellular replication and are used in the treatment of various malignancies, especially those involving rapidly proliferating neoplasms (new growth). Some injectable antimetabolites include methotrexate and fluorouracil. Methotrexate is also available orally and has been used for severe, resistant cases of psoriasis, rheumatoid arthritis, and lupus. Fluorouracil is also available in a topical formulation (Efudex) to treat certain skin cancers.

One of the newer antimetabolite agents is gemcitabine (Gemzar), which is used to treat multiple types of cancer, including those affecting the pancreas, lungs, bladder, breasts, and ovaries. Among other newer drugs in this class are capecitabine and raltitrexed.

Tissues that have a high rate of cellular metabolism, such as neoplasms, hair follicles, buccal and GI tract lining, fetal cells, and bone marrow, are most sensitive to the effects of the antimetabolites, which account for the side effects and cautions listed here.

Note

Leucovorin (a reduced form of folic acid) is sometimes used as a "rescue agent" following methotrexate administration to reduce the side effects of methotrexate-induced hematological and GI toxicity.

Side effects of antimetabolites can include the following:

- ❗ Anorexia, nausea, vomiting, and diarrhea
- ❗ Ulceration and bleeding of the oral mucosa and GI tract
- ❗ Bone marrow suppression
- ❗ Rash, itching, photosensitivity, and scaling

Cautions/contraindications with antimetabolites apply to:

Renal and hepatic disorders
Pregnancy
GI ulcers

Clinical Connection

Methotrexate Dosing

Many oral chemotherapy medications are administered on a daily basis, whereas methotrexate is *only* dosed once weekly; it is generally given as multiple 2.5-mg tablets on the same day each week. This special dosing schedule is to allow the body to recover from the various side effects. Often, folic acid is given on the days that the patient is not taking methotrexate to help alleviate side effects as well. It is important to educate patients that to ensure their treatment is successful and safe, methotrexate is *not* taken daily like some of their other pills.

Alkylating Agents

Alkylating agents are used in the treatment of a wide range of cancers. Some alkylating agents include cisplatin and cyclophosphamide. Trabectedin (Yondelis) is the newest alkylating agent and is used in the treatment of sarcomas and ovarian cancer that is resistant to traditional treatment.

These agents prevent cell growth by damaging DNA needed for reproduction. They can cause long-term damage to the bone marrow. In a few rare cases, this damage can eventually lead to acute leukemia 5–10 years after treatment.

Side effects of alkylating agents can include the following:

- ❗ Mucosal ulceration; bone marrow suppression, including leukopenia with infection; anemia; and thrombocytopenia with hemorrhage
- ❗ Neurotoxicity, including headache, vertigo, and seizures
- ❗ Hemorrhagic cystitis with cyclophosphamide (mesna, a chemoprotectant, can be administered prior to chemotherapy to prevent this toxicity)
- Rash and alopecia
- Pulmonary fibrosis
- Necrosis of tissue if intravenous (IV) drug solution infiltrates into tissues (for IV cannula placement, avoid areas of previous irradiation and extremities with poor venous circulation)

Cautions/contraindications with alkylating agents apply to:

- Patients in a severely weakened state
- Pregnancy
- Renal disease (with cisplatin—major dose-limiting toxicity)

Mitotic Inhibitors

Mitosis refers to the process of cell division and reproduction. Mitotic inhibitors are often plant alkaloids and other compounds derived from natural products that block mitosis when it is occurring in an uncontrolled way. They are used to treat many different types of cancer. These agents are also known for their potential to cause peripheral nerve damage and myelosuppression, which can be dose-limiting side effects. **Dose-limiting side effects** are those side effects that are serious enough to prevent increasing the dose or level of treatment.

Plant Alkaloids

Plant alkaloids, for example, vinblastine and vincristine, which are derived from the periwinkle plant, are used in combination with other chemotherapeutic agents in the treatment of various malignancies. Vinorelbine (Navelbine), a semisynthetic agent derived from vinblastine, has been recommended as a treatment of choice for lung cancer in older patients.

Side effects of plant alkaloids can include the following:

- ❗ Neurotoxicity
- ❗ Severe constipation or diarrhea, nausea, and vomiting
- ❗ Oral or GI ulceration
- ❗ Rash, phototoxicity (increased reaction to sunlight), and alopecia
- Leukopenia with vinblastine
- Necrosis of tissue if IV drug solution infiltrates into tissues (for IV cannula placement, avoid areas of previous irradiation and extremities with poor venous circulation)

Cautions/contraindications with plant alkaloids apply to:

- Pregnancy
- Hepatic dysfunction
- Infection
- Older adult patients

Note

Intrathecal administration (into the spinal canal) of these agents is fatal. This route must not be used. Syringes containing these agents should be labeled "Warning—For IV use only, fatal if given intrathecally."

Taxanes

Paclitaxel, another plant alkaloid, was originally extracted from the bark of the Western (Pacific) yew. It is structurally different from other available antineoplastic agents. It is used as a second-line or subsequent therapy in patients with metastatic breast or ovarian carcinoma refractory to conventional chemotherapy. Cabazitaxel (Jevtana), another taxane, is used in hormone-refractory metastatic prostate cancer.

Adverse side effects of paclitaxel are frequent and include:

- ❗ Bone marrow suppression
- ❗ Hypersensitivity reactions
- ❗ Peripheral neuropathy (occurs in up to 30% of patients)
- ❗ Nausea, vomiting, diarrhea, and mucositis
- ❗ Alopecia
- ❗ Necrosis of tissue if IV drug solution infiltrates into tissues

Cautions/contraindications with paclitaxel apply to:

- Pregnancy
- Hepatic dysfunction
- Infection
- Cardiac disease

Because of its severe adverse reactions, paclitaxel is administered only by IV under the constant supervision of an oncologist, with frequent monitoring of vital signs and facilities available for emergency interventions if required.

NAB-paclitaxel (Abraxane) was the first approved albumin nanoparticle drug. Paclitaxel is mixed with albumin nanoparticles (one-billionth of a meter in size), which act as biological delivery agents to transport the drug to the needed site of action. Refer to Figure 26-2 for a rendering of how nanoparticles work.

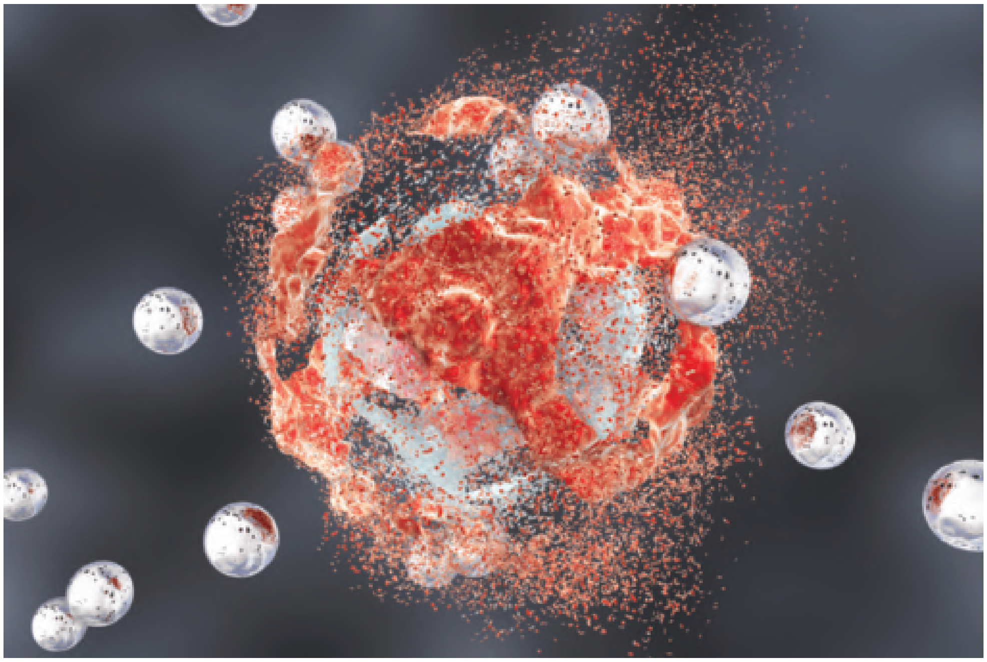


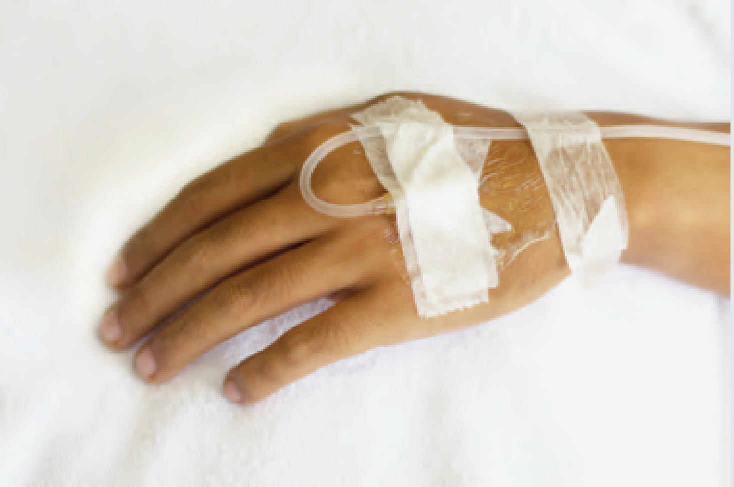
Figure 26-2 Illustration of nanoparticles attacking and destroying a tumor cell.

Kateryna Kon/Shutterstock.com.

Clinical Connection

Extravasation

Extravasation occurs when a drug or liquid intended for IV administration leaks into the surrounding tissue (Figure 26-3). In particular, chemotherapy can cause painful irritation which, if left untreated, can lead to necrosis of the tissue. In addition to various treatment options, extravasation can also be relieved by using a cold or warm compress. Different chemotherapy agents are relieved better by one or the other. Whereas warm compresses work better for plant (vinca) alkaloids and taxanes, cold compresses work better for anthracyclines, other alkylating agents, and antitumor antibiotics. Educating the patient on which to use could make a major difference in their level of relief.



Supoj Pongpancharoen/Shutterstock.com.

Figure 26-3 When a fluid leaks out of the vein and into the surrounding tissue, necrosis of that tissue can occur. The health care professional must be vigilant in monitoring the IV site to watch for swelling or pain, as this site is showing early signs of swelling.

Antitumor Antibiotics

Antitumor antibiotics are used to treat a wide variety of malignancies. Doxorubicin (Adriamycin) is considered the most active chemotherapy agent and is a critical component in the treatment protocols of breast, lung, gastric, and ovarian cancers and lymphoma, but it can permanently damage the heart if a maximum lifetime dose is reached. This means that regardless of the effectiveness, these medications can only be used for a set period of time. Daunorubicin (Cerubidine), which is structurally related to doxorubicin, is primarily used for acute leukemias because of its lower incidence of cardiotoxicity. Other antitumor antibiotics include bleomycin and mitomycin. They are frequently used in combination with other drugs.

Side effects of antitumor antibiotics can include the following:

- Anorexia, nausea, vomiting, and diarrhea
- Bone marrow suppression (the acute dose-limiting toxicity with doxorubicin and daunorubicin)
- Cardiotoxicity, including arrhythmias; congestive heart failure; and cardiomyopathy (cumulative dosing with most medications except bleomycin)
- Pneumonitis and dyspnea; pulmonary fibrosis with bleomycin
- Ulceration of the mouth or colon
- Alopecia, rash, and scaling
- Tissue necrosis if IV solution infiltrates

Note

Side effects vary depending on specific medications. Always check side effects for each drug in this classification.

Cautions/contraindications with antitumor antibiotics apply to:

Pregnancy
Liver disorders
Cardiac disease, especially congestive heart failure

Hormones and Hormone Modifiers

Hormones used in the treatment of cancer include the corticosteroids. Hormone modifiers include the antiestrogen and the antiandrogen agents.

Corticosteroids

Corticosteroids, such as prednisone, are used primarily for their suppressant effect on lymphocytes in leukemias and lymphomas. They are also frequently used in combination with other chemotherapeutic agents in the treatment of some types of cancer and before chemotherapy to help prevent severe allergic reactions. In addition, large doses of dexamethasone, when administered before or during chemotherapy, have been found to be effective in the prevention and treatment of nausea and vomiting associated with many antineoplastic agents. Dexamethasone is also used to treat cerebral edema associated with brain tumors.

Side effects with prolonged use of corticosteroids include:

- ❗ Fluid retention, edema
- ❗ Osteoporosis with fractures (long-term use)

Antiestrogens

A *nonsteroidal* agent belonging to a class of drugs called selective estrogen-receptor modifiers (SERMs), tamoxifen, binds to estrogen receptors in various tissues. It can be used as a primary hormonal therapy for metastatic estrogen receptor–positive breast cancer in both males and postmenopausal females as well as for palliative treatment. Tamoxifen also stimulates estrogen receptors in bones and may help prevent osteoporosis.

Serious adverse side effects are rare and usually dose-related. Nausea, vomiting, hot flashes, and night sweats can occur in up to 66% of cases, but these usually do not require discontinuation of the medication. Antidepressants may be prescribed to alleviate tamoxifen-associated hot flashes. Some antidepressants may reduce the potency of tamoxifen.

Anastrozole (Arimidex) and letrozole (Femara), which inhibit the final step in estrogen production, offer alternatives to tamoxifen in postmenopausal females with breast cancer. They can also cause nausea, vomiting, and hot flashes similar to tamoxifen but are more likely than tamoxifen to cause osteoporosis.

Antiandrogens

Antiandrogen drugs include leuprolide acetate, which suppresses testosterone production in the testes and is usually administered intramuscularly (IM) (Lupron Depot) or subcutaneously (SC) (Eligard) on monthly regimens (every 1, 3, 4, or 6 months, depending on the dosage) for prostate cancer. They are also used as hormonal therapy in the treatment of endometriosis.

Bicalutamide (Casodex) is an oral nonsteroidal antiandrogen that interferes with the binding of testosterone to androgen receptors in the prostate and is used simultaneously with leuprolide in the treatment of metastatic prostate cancer.

Side effects of antiandrogens can include:

- ❗ Impotence
- ❗ Hot flashes, generalized pain, infection, constipation, and nausea

Sex hormones, including the estrogens, progestins, and androgens, are also used as antineoplastic agents in the treatment of malignancies involving the reproductive system (e.g., cancer of the breast, uterus, or prostate).

Biological Therapies

Biological therapies (also called immunotherapies, biotherapies, or biological response modifier therapies) are designed to repair, stimulate, or enhance cancer patients' natural immune systems to more effectively recognize and attack cancer cells. Some therapies are used to lessen the side effects caused by certain cancer treatments. There are different types of immunotherapy: the *active* or *direct* type (such as interferons) stimulates the body's own immune system to fight the disease. The *passive* or *indirect* type (such as monoclonal antibodies or MABs) uses immune system components created outside the body.

Interferons

Interferon alfa (Intron A), which is the type most widely used in cancer treatments, is a complex combination of many proteins that boost immune system response. Interferons are used in the treatment of certain leukemias, melanoma, Kaposi's sarcoma, and non-Hodgkin's lymphoma. Interferons are also used to treat hepatitis B and C, multiple sclerosis, and other conditions.

Adverse side effects of interferons, sometimes severe, are experienced by almost all patients receiving interferon, varying with the dosage and condition. Most common side effects include:

- ❗ Flulike syndrome—fever, fatigue, chills, headache, muscle aches, and pains
- ❗ GI symptoms—anorexia, nausea, vomiting, diarrhea, and dry mouth
- ❗ Nervous system effects—sleep disturbances, depression, and neuropathy
- ❗ Hematological effects—especially leukopenia and anemia
- Dyspnea, cough, nasal congestion, and pneumonia
- Alopecia—transient

Colony-Stimulating Factors (CSFs)

CSFs such as erythropoietin (Epogen, Procrit) usually do not directly affect tumor cells. They encourage bone marrow stem cells to divide and develop into red blood cells (RBCs), white blood cells (WBCs), and platelets. Because anticancer drugs can damage the body's ability to make these cells, patients have an increased risk of developing infections, becoming anemic, and bleeding more easily. By using CSFs to stimulate blood cell production, oncologists can increase the doses of antineoplastics without increasing the risk of infection or the need for transfusions. CSFs are also used to increase the counts of RBCs and WBCs so that chemotherapy can continue, as treatments are often delayed if counts drop too low.

Monoclonal Antibodies (MABs)

MABs are *exogenous* (outside of body) antibodies genetically engineered in the laboratory. MABs are designed to target only cancer cells, thereby sparing normal tissues (i.e., they are not *directly* cytotoxic). This reduces host toxicity while simultaneously increasing toxicity to cancer cells. One specific type of MAB is indicated where tumors have rich blood supplies, which can facilitate their growth and spread. Angiogenesis inhibitors (AIs) prevent the formation of new blood vessels that tumors need to grow and invade nearby tissue. Bevacizumab (Avastin), in combination with other agents, is indicated for the first-line treatment of patients with metastatic carcinoma of the highly vascularized colon, kidney, or lung. AIs may only stop or slow the growth of a cancer, not completely eradicate it.

Another MAB, trastuzumab (Herceptin), combined with paclitaxel, is indicated for first-line treatment of metastatic breast cancer in patients with tumors that produce excess amounts of a protein called HER2. *All MABs are administered intravenously.*

Side effects of MABs are common, especially with the first infusion, and can include:

- ❗ Fever and chills, headache, and dizziness
- ❗ Nausea and vomiting
- Itching, rash, and generalized pain

These reactions should occur less frequently with subsequent infusions.

Severe reactions can be minimized by *premedicating* with acetaminophen (Tylenol), diphenhydramine (Benadryl), and/or meperidine (Demerol). AIs (Avastin) may have side effects that are different from other MABs. Signs of severe reaction can include:

- ❗ Angioedema, hypotension, dyspnea, and bronchospasm (may be necessary to stop infusion)
- ❗ Hypersensitivity reactions (including anaphylaxis)
- ❗ Cardiac arrhythmias, angina, heart failure, cardiomyopathy; hypertensive crisis (with Avastin)
- ❗ Acute renal failure (not with Herceptin)
- ❗ Hematological toxicity (i.e., reduced WBCs); complete blood count and platelet count should be monitored frequently
- ❗ GI perforation, GI bleed; impaired wound healing (all with Avastin)

Targeted Therapies

Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression. By focusing on molecular and cellular changes that are specific to cancer, targeted cancer therapies may be more effective than other types of treatment, including chemotherapy and radiotherapy, and are less harmful to normal cells.

Signal Transduction Inhibitors

One of the newer and largest groupings of targeted therapy drugs is called the STIs, which block specific enzymes and growth factor receptors that signal cancer cell proliferation. Imatinib (Gleevec) is one of the first clinically useful agents in this class and is approved for the treatment of chronic myelogenous leukemia and some rare types of cancers. The majority of STIs are given by the *oral* route. Side effects vary greatly depending on the indication, agent, and combination therapy used.

Vaccines

Vaccines are medicines that boost the immune system's natural ability to protect the body against "foreign invaders," mainly infectious agents that may cause disease. There are two broad types of cancer vaccines:

- *Preventive (or prophylactic),* which are intended to prevent cancer from developing in healthy people
- *Treatment (or therapeutic),* which are intended to treat an existing cancer by strengthening the body's natural defenses against the cancer

Gardasil is approved by the Food and Drug Administration (FDA) to *protect* against infection by the strains of human papillomavirus (HPV) that cause approximately 70% of all cases of cervical cancer worldwide. The vaccine is also effective at preventing other kinds of cancer, including anal and oropharyngeal, that are caused by HPV. The vaccine is not indicated for the *treatment* of HPV infection, nor will it protect against all HPV types not contained within the vaccine. Therefore, recipients of the vaccine should continue to undergo routine cervical and annual cancer screenings (Figure 26-4). It should be noted that although the vaccine is largely marketed to prevent cervical cancer, it is recommended that both males and females are vaccinated because the incidence of cancer is equal between the two sexes. Males experience a higher incidence of anal and oropharyngeal cancers, while females experience a higher incidence of ovarian cancer.

BlurryMe/Shutterstock.com.

Figure 26-4 Young adults are encouraged to get Gardasil to help prevent the spread and incidence of these preventable types of cancer.

The first cancer *treatment* vaccine, sipuleucel-T (Provenge), was approved for use in some males with metastatic prostate cancer. Sipuleucel-T is made from a patient's WBCs to stimulate the patient's immune system against the cancer and is manufactured for each patient individually.

T-VEC (Imlygic) is another vaccine treatment. It is a virus-based vaccine that is used to treat advanced melanoma that cannot be completely removed with surgery.

It is made of a virus that has been genetically modified to promote an anticancer immune response.

Radioactive Isotopes

Radioactive isotopes are also used in the treatment of certain types of cancer. Sometimes the radioactive material is injected into the affected site (e.g., radiogold, which is injected into the pleural or peritoneal cavity to treat the abnormal accumulation of fluid called ascites caused by the cancer). Radioactive sodium iodine is administered PO to treat thyroid cancer (thyroid cells naturally take up radioactive iodine). Radioactive material is sometimes implanted in the body in the form of capsules, needles, or seeds.

The newest targeted therapy provides the added benefit of radiation. Radioimmunotherapy consists of MABs that have radioisotopes attached to them so that whatever the targeted antibody binds to can also be irradiated. Tositumomab (Bexxar) with iodine-131 is indicated for patients with refractory non-Hodgkin's lymphoma. The primary side effect after radioimmunotherapy is a decreased blood count occurring 4 to 6 weeks after treatment. The counts remain low for 2 to 3 weeks and then return to normal. The distinct advantage of radioimmunotherapy is that it is usually given one time.

Health care professionals caring for patients receiving radioactive isotopes must observe special precautions to prevent unnecessary radiation exposure. Gowns and gloves should be worn when handling patient excreta such as feces, urine, and body secretions. Other isolation procedures, such as handling of linens, will be outlined in the facility's procedure manual. This protocol should be followed with great care by all those who come in contact with patients receiving radioactive materials, for the protection of patients as well as health care professionals.

Cautions and Responsibilities for Antineoplastic Drugs

Health care professionals involved in the administration of antineoplastic agents, as well as those who care for these patients, have a number of very important responsibilities:

1. All medications should be given on time and exactly as prescribed to keep the patient as comfortable as possible and maximize the efficacy and safety of the medication. Check package inserts on all new drugs.
2. IV sites must be checked with great care because some antineoplastic agents (especially antitumor antibiotics and vinca alkaloids) can cause extreme tissue damage and necrosis if infiltration into surrounding tissues occurs. (Gloves should be worn when handling IVs with antineoplastic agents.) Facilities may have a kit available containing supplies and medications needed to treat extravasation.
3. IV fluids containing antineoplastic agents should not be allowed to get on the skin or into the eyes of the patient or the one administering the medication. Flush skin or eyes copiously if spills occur.

4. Antiemetics should be immediately available and administered as prescribed to minimize nausea and vomiting. Ondansetron (Zofran) and dolasetron (Anzemet) are examples of antiemetics used for this purpose.
5. Careful and frequent oral hygiene is essential to minimize discomfort and ulceration.
6. Soft foods and cool liquids should be available to the patient as required.
7. Accurate intake and output is important for the adequate assessment of hydration.
8. Careful observation and reporting of symptoms and side effects is an essential part of chemotherapy care.
9. Aseptic technique is necessary to minimize the chance of infection in patients with reduced resistance to infection.
10. Careful assessment of vital signs is important to identify the signs of infection, cardiac irregularities, and dyspnea.
11. The family and health care professional must be informed about all aspects of chemotherapy and answer the patient's questions honestly. Awareness of verbal and nonverbal communication that gives clues to the patient's needs is absolutely necessary.
12. Careful attention to detail, astute observations, appropriate interventions, and compassion are an integral part of care when the patient is receiving chemotherapy.
13. The health care professional should reassure the patient that someone will be available to help at all times and should identify all resources available for both the patient and their family.

Refer to Table 26-2 for a summary of antineoplastic agents' side effects.

Patient Education

Patients being treated with antineoplastic drugs and their families should be instructed regarding:

Side effects to expect, how long they can be expected to continue, and that they are frequently temporary

Comfort measures for coping with unpleasant side effects (e.g., antiemetics and antidiarrheal agents as prescribed)

Appropriate diet with foods that are more palatable and more likely to be tolerated (e.g., soft foods; bland foods; a variety of liquids; and especially cold foods in frequent, small quantities)

Careful aseptic technique to decrease the chance of infections and reporting any signs of infection (e.g., fever)

Careful oral hygiene with swabs to prevent further trauma to ulcerated mucosa

Observation for bruises as well as bleeding in stool, urine, and gums, and reporting this to medical personnel

Reporting any persistent or unusual side effects, such as dizziness, severe headache, numbness, tingling, difficulty walking, or visual disturbances

Available community resources to assist and support the patient (e.g., cancer society, hospice, or home health services) as required and recommended by the physician

How to obtain information and answers to questions regarding treatment

The right of patients to terminate therapy if they wish

Table 26-2 Side Effects of Antineoplastic Agents

	Drug Categories							
Possible Side Effects	**Antimetabolites**	**Alkylating Agents**	**Mitotic Inhibitors (Plant Alkaloids)**	**Antitumor Antibiotics**	**Hormone and Hormone Modifiers**	**Interferons**	**Monoclonal Antibodies**	**Signal Transduction Inhibitors**
GI effects: nausea, vomiting, diarrhea	X	X	X	X	X	X	X	X
Alopecia	X	X	X	X		X		
Suppressed bone marrow	X	X	X	X		X (especially leukopenia)	X	
Ulcerated mucosa	X	X	X	X			X	
Photosensitivity	X		X					
Neurotoxicity	X	X	X			X		
Hypersensitivity			X				X	X
Cardiotoxicity				X			X	X
Respiratory dysfunction	X	X		X		X	X	X
Hot flashes					X			
Impotence					X			
Flulike syndrome						X	X	X
Renal toxicity		X					X	X
Extravasation		X	X	X				

Cytotoxic Drug Dangers to Health Care Professionals

Most cytotoxic drugs are toxic substances known to be carcinogenic, mutagenic, or teratogenic. Anyone who prepares, administers, or cares for patients receiving cytotoxic drugs should be aware of the dangers involved. It is essential that policies and procedures be followed exactly as outlined on the labels provided by the drug company. Guidelines of the individual health care agency must also be followed to the letter for the safety of all concerned.

The danger to health care professionals from handling a hazardous drug stems from a combination of its inherent toxicity and the extent to which health care professionals are exposed in the course of carrying out their duties. This exposure may be from inadvertent ingestion of the drug on foodstuffs, inhalation of drug dust or droplets, or direct skin contact.

Recommended safe handling methods include four broad goals:

1. Protect and secure packages of hazardous drugs. Store them separately from nonhazardous drugs.
2. Inform and educate all involved personnel about hazardous drugs and train them in safe handling procedures.
3. Do not let the drugs escape from containers when they are manipulated (i.e., dissolved, transferred, administered, or discarded).
4. Eliminate the possibility of inadvertent ingestion or inhalation and direct skin or eye contact with the drugs.

Specific recommendations for cytotoxic drugs include the following:

1. When preparing these drugs, wear gloves, long-sleeved gowns, splash goggles, and disposable respirator masks.
2. For administration, wear long-sleeved gowns and gloves. Syringes and IV sets with Luer-Lock fittings should be used, and care should be taken that all fittings are secure.
3. Dispose of syringes, IV tubing and bags, gauze, and any other contaminated material such as linens in a leak-proof, puncture-resistant container that is labeled “HAZARD.”
4. Wear gloves and gown when handling excreta from patients receiving cytotoxic drugs.
5. Those who are pregnant, breastfeeding, or actively trying to conceive a child should not care for patients receiving cytotoxic drugs.

For more detailed instructions, refer to *ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs,* which is reproduced in the *AHFS Drug Information* book and updated based on information from the Occupational Safety and Health Administration (OSHA), National Institutes of Health (NIH), National Study Commission on Cytotoxic Exposure, and American Medical Association (AMA) Council on Scientific Affairs.

Antineoplastic therapy is complex and changes frequently with ongoing research. Therefore, you are not expected to remember the names of all of the antineoplastic agents. However, you need to know the *common side effects, interventions, cautions, and appropriate patient education*.

Case Study A

Antineoplastic Drugs

During a patient's annual physical, their physician palpates the patient's swollen thyroid gland. A CT scan and biopsy determine that the patient has thyroid cancer. The physician refers the patient to an oncologist, who indicates that they should be treated with radioactive sodium iodide, a radioisotope.

1. This category of drug is called a(n):
   a. Colony-stimulating factor
   b. Vaccine
   c. Angiogenesis inhibitor
   d. Signal transduction inhibitor

2. Upon receiving their first dose, the nurse informs the patient that they can expect which symptom(s)?
   a. Fever and chills
   b. Hot flashes
   c. Decreased platelet count
   d. Blood in his stools

3. Prior to a first dose, the nurse will administer which medication to minimize a potentially severe reaction?
   a. Morphine sulfate
   b. Motrin
   c. Mylanta
   d. Benadryl

4. During an infusion of Avastin, the patient will be monitored for which possible side effect that may necessitate stopping the infusion?
   a. Nausea
   b. Bronchospasm
   c. Metallic taste in the mouth
   d. Headache

5. In the next several weeks, the patient will be monitored for which side effect?
   a. Hypotension
   b. Low WBCs
   c. Constipation
   d. Excessive bruising

Case Study B

Antineoplastic Drugs

A patient has a new diagnosis of metastatic colon cancer. The oncologist has ordered a medication from a category of drugs as a first-line treatment that will *not* eradicate the cancer but *will* stop or slow the growth of cancer.

1. By which route will this specific radioisotope be administered?
   a. IM injection
   b. Seed placement
   c. Orally
   d. Intravenously

2. What is a distinct advantage of radioimmunotherapy?
   a. It is usually given one time.
   b. It has no side effects.
   c. It is given once a month.
   d. No extra precautions need to be taken post-treatment.

3. Which of the following is the primary side effect of radioimmunotherapy?
   a. Diarrhea
   b. Nausea
   c. Fever
   d. Decreased blood count

(*Continued*)

4. What should the nurse wear when handling patient excreta after radioimmunotherapy?

a. Gloves only
b. Gown and gloves
c. Cap, gown, and gloves
d. Cap, gown, gloves, and booties

5. Suppose that the patient develops a low blood count. What category of drug would be given to stimulate bone marrow production of RBCs, WBCs, and platelets?

a. Colony-stimulating factor
b. Hormone modifiers
c. Biological therapy (interferons)
d. Antitumor antibiotics

Chapter Review Quiz

Match the term with the definition.

1. _______ Palliative
2. _______ Cytotoxic
3. _______ Antineoplastic
4. _______ Monoclonal antibodies
5. _______ Proliferating
6. _______ Exogenous antibodies
7. _______ Refractory
8. _______ Immunosuppressive
9. _______ Endogenous antibodies
10. _______ Clone

a. Target only **cancer cells**
b. Unresponsive to treatment
c. Within the cell
d. Produce a copy
e. Decreases antibody production
f. Alleviation of symptoms
g. Engineered in a laboratory
h. Reproducing rapidly
i. Destructive to cells
j. Counteracts malignant cell growth

Multiple Choice

11. Alkylating agents such as cisplatin and cyclophosphamide work by which method of action?

a. They prevent growth by damaging the DNA needed for reproduction.
b. They assist in bone marrow depression.
c. They block cell mitosis.
d. They bind to estrogen receptors.

12. A tumor that is classified as benign is:

a. Destructive to other cells
b. Noncancerous
c. Cancerous
d. Resistant to radiation

13. A common side effect of an antimetabolite is:

a. Numbness and tingling
b. Phototoxicity
c. Nausea and vomiting
d. Visual disturbances

14. Which drug is used to treat cerebral edema associated with brain tumors?

a. Leucovorin
b. Anastrozole
c. Letrozole
d. Dexamethasone

15. Which antitumor antibiotic is known to be cardiotoxic and should not be used in patients with congestive heart failure unless no other options are possible?

a. Mitomycin
b. Daunorubicin
c. Adriamycin
d. Bleomycin

Chapter 27

Age-Related Medication Issues

Key Terms and Concepts

Beers list drugs

Comprehensive medication review (CMR)

Cumulative effects

Medication-related problems (MRPs)

Medication therapy management (MTM)

Mental impairment

Motor impairment

Nonadherence

Polypharmacy

Paradoxical effect

Potentially inappropriate medications (PIMs)

Objectives

Upon completion of this chapter, the learner should be able to:

1. List medications that are inappropriate for older adults and describe how to access updated information.
2. Describe four factors that may lead to cumulative effects in older adults.
3. Identify classes of medications that frequently cause adverse side effects in older adults.
4. Explain the dangers of NSAID therapy and other medications that have gastrointestinal complications.
5. Describe medication classes that can contribute to syncope or falls.
6. Describe patient education for all patients on long-term drug therapy.
7. Describe the impact of polypharmacy on older adults and how to combat it.
8. Describe the special considerations for pediatric medications.
9. Describe pediatric medication considerations.

Age can play an important role in how medications affect patients and how they are distributed in the body. Younger individuals and older adults may experience different levels of effectiveness, increased or decreased side effects, and even opposite effects from the same medication when given to the average adult. A **paradoxical effect** is when a medication has the opposite effect on a person (or group of persons) compared to average adults. One example is diphenhydramine, which is an antihistamine that causes drowsiness in most adults. Many children experience the opposite effect and become more alert, awake, and even agitated. Regardless of the effects, special medication considerations must be made for older adult, pediatric, and adolescent patients to ensure they receive safe and effective drug therapy.

Older Adult Considerations

Today, people are living longer and are taking more medications. In the United States, almost 90% of older adults regularly take at least 1 prescription drug, 80% regularly take at least 2 prescription drugs, and nearly 40% regularly take at least 5 different prescription drugs., Many add over-the-counter (OTC) medications and supplements to their prescription medications as well. Consequently, there has also been an increase in serious complications resulting from adverse drug reactions. It has been estimated that about 50% of hospitalizations because of adverse drug effects are in older adults and that **medication-related problems (MRPs)** cause approximately 100,000 deaths annually.

MRPs can be mistaken for what is often considered a normal consequence of aging or for progression of disease. Cognitive impairment and behavioral changes are frequently the result of drug therapy. Therefore, it is imperative that members of the health care community work together to reverse this dangerous trend.

The aging process is an individualized matter. Because of genetic and environmental factors as well as good health practices—for example, exercise, healthy diet, and mental stimulation—some older adults may not feel or appear particularly different from younger people. However, we need to realize that there are gradual changes in our body composition and organ function as we grow older. These changes can affect the reaction to drugs and make the individual more sensitive to a wide variety of medications.

Physiologic Changes with Increasing Age

Complex changes of aging involve both anatomic and physiological factors that affect how drugs are processed in the body. The four processes that drugs undergo in the body—that is, **absorption**, **distribution**, **metabolism** (biotransformation), and **excretion**—are all altered as the body ages. The result of these slowed processes can be exaggerated responses to medications, changes in drug levels, increased susceptibility to drug–drug interactions, and a 3- to 10-fold risk of adverse drug reactions compared with younger individuals.

Cumulative effects of drugs in older adults can be because of:

- Inadequate absorption—slowed gastrointestinal (GI) motility, reduced fluid intake, and/or relative achlorhydria (lack of stomach acid)
- Impaired distribution—circulatory dysfunction, less muscle, and more fat
- Slower metabolism—hepatic dysfunction
- Impaired excretion—renal dysfunction, constipation, or poor exchange of gases in the lungs

Absorption

As we age, several changes happen to our GI tract. Not only does gastric motility decrease, but gastric acid production diminishes, increasing gastric pH, causing a more alkaline environment, which affects the absorption process. Many older adults also take medication that reduces gastric acid, for example, famotidine (Pepcid) or omeprazole (Prilosec).

Antacids are also used frequently by older adults. Calcium, magnesium, and aluminum form insoluble and nonabsorbable complexes that are passed out of the body in the feces. Some of the drugs that are affected by antacids are quinolone antibiotics, tetracycline, iron salts, ketoconazole, and isoniazid. Therefore, it is recommended that these, and certain other drugs as well, not be taken within 2 h of taking antacids.

Decreased gastric motility, especially when taking anticholinergic drugs, for example, the tricyclic antidepressants and the antispasmodics, can cause adverse effects. Gastric slowing leads to increased time for other drugs to be dissolved and absorbed.

Absorption by other routes of administration may be affected as well. Aging skin atrophies and becomes thinner, potentially impairing transdermal drug absorption of patches and gels because of reduced blood flow to the skin. Muscle mass may be significantly decreased in some older adult patients, which may alter drug absorption of IM and subcutaneous injections.

Distribution

Once drugs are absorbed and enter the circulation, many of them bind to proteins. Albumin is the principal protein used to bind drugs. As we age, the liver produces less albumin, especially in conditions such as malnutrition, cancer, diabetes, surgery, burns, and liver disease. This allows more of the drug to be unbound (free) to reach receptor sites and therefore have a greater-than-expected response.

Phenytoin (Dilantin) is an example of a drug that responds quite noticeably to drops in plasma albumin levels. Older adults need to be monitored frequently with laboratory studies, especially with symptoms such as sleepiness, confusion, nystagmus (involuntary back-and-forth eye movements), diplopia, and ataxia. Other drugs that are highly protein bound include warfarin, aspirin, naproxen, diazepam, and valproic acid (Depakote). When any of these drugs are used in the older adult, the best advice is to start at the lowest effective dose and increase slowly to avoid adverse effects. The frequency of administration may also need to be decreased.

Water accounts for approximately 60% of body weight in healthy young individuals but accounts for only 45% in healthy older adults. Because the older adult has less body water, drugs that are water soluble, such as digoxin, ethanol, lithium, morphine, and theophylline, may become concentrated and cause adverse reactions, with additive effects over time. Smaller doses would be needed to avoid potential toxicity.

Metabolism

The liver serves as a major site for drug metabolism. As we age, the mass of functional liver tissue and blood flow to the liver decreases. The ability of the liver to break down drugs declines, and drugs remain in the body longer. Repeated dosing can result in the accumulation of the drug and increases the risk for toxicity. Some drugs that can produce toxic effects when poorly metabolized are caffeine, diazepam, chlordiazepoxide, lidocaine, theophylline, meperidine, hydromorphone, warfarin, phenytoin, diphenhydramine, and propranolol.

All benzodiazepines increase the risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults. Older adults have an increased sensitivity to all benzodiazepines and decreased metabolism of long-acting agents. As a result, these drugs build up with repeated administration and cause *side effects,* such as daytime sedation, dizziness, lethargy, and ataxia. Therefore, it may be necessary to consider selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), or buspirone as alternatives for anxiety, and short-term use of zolpidem (Ambien) as an alternative for hypnotics. If a benzodiazepine must be used, older adults should be given one of the "LOT" benzodiazepines, as they are more easily metabolized and do not accumulate as readily. LOT stands for lorazepam, oxazepam, and temazepam and they show these cognitive effects and risks to a lesser extent.

Omeprazole (Prilosec) and cimetidine (Tagamet) inhibit liver enzymes from breaking down the long-acting benzodiazepines and prolong the drug's duration of action. It may be preferable to use other proton pump inhibitors (PPIs) or histamine$_2$ (H_2) blockers such as pantoprazole (Protonix) or famotidine (Pepcid) rather than omeprazole or cimetidine.

Excretion

In the older adult, kidney size, blood flow, and glomerular filtration all decrease, resulting in a decline in creatinine clearance. Illnesses such as hypertension, heart failure, and diabetes add to the age-related loss and further reduce creatinine clearance. Consequently, drug by-products normally eliminated through the kidneys can accumulate, with toxic effects. For example, digoxin poses increased risks of adverse reactions (e.g., arrhythmias) to older adults with impaired renal function.

Nephrotoxic drugs, such as the aminoglycosides, can prove particularly dangerous to older people with reduced renal function. Acute renal failure and irreversible damage to the eighth cranial nerve (auditory and vestibular branches) are possible.

Older Adults and Drug Development

Although age-related physiological changes affect how older adults process and tolerate medications, pharmaceutical research is frequently focused on younger individuals; older adults are often excluded from, or underrepresented in, clinical trials. The study results may be inappropriately extrapolated to other populations, with negative outcomes.

An example of this was a study in which spironolactone was found to reduce mortality in clinical trial patients who were around 60 years old. When this finding was extrapolated to the general population, where most patients with heart failure are older than 75 years, there was an increase in hyperkalemic deaths and no change in heart failure hospitalizations.

Some medicines that are perfectly safe for a 30-year-old person may produce unexpected results in a person over age 50 or 60 years. An example is *digoxin* (*Lanoxin*). An older person still on the same dose that was appropriate 10 or 20 years earlier may experience *side effects* such as loss of appetite, weakness, personality changes, nightmares, confusion, or even hallucinations. In addition, digoxin can interact with many other drugs, sometimes slowing the clearance of the drug from the system; this could result in cumulative effects, including possible dangerous arrhythmias.

Potentially Inappropriate Medication Use in Older Adults

A group of physicians led by Dr. Mark Beers conducted a national survey of geriatric experts in 1991 to determine the most *inappropriate* drugs for ambulatory nursing home residents and adults 65 years or older. Medications were considered inappropriate if there was evidence in the literature to substantiate that the risk of drug use outweighed the clinical benefit when alternative therapy was available. The results of this survey came to be called the *Beers list* (**Beers list drugs**).

The Beers study was updated and revised by another panel of experts, and the results were introduced first in 1991, and published most recently in 2023 in the *Journal of the American Geriatrics Society* under the title "Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults." The goal of this list is to improve care for older adults by reducing their exposure to **potentially inappropriate medications (PIMs)**. Keep in mind that the criteria are not applicable in all circumstances (e.g., patients receiving palliative and hospice care).

The complete article concerning the development of the Beers list and additional reference tables with rationale is available for free download from http://www.americangeriatrics.org.

Health care professionals treating older adults should have ready access to the Beers list and recognize the common classes of medications that can produce problems. For example, according to a recent study from the Centers for Disease Control and Prevention (CDC), improper antidiabetic and antithrombotic drug therapy is responsible for more than two-thirds of drug-related hospitalizations in older patients. Focusing on improving the management of antithrombotic and antidiabetic drugs is most likely to have sizable, clinically significant, and measurable effects.

Drugs to Avoid with Certain Medical Conditions

Many of the medications on the Beers list have anticholinergic properties and are not recommended for use in the older adult population. Older adults become very sensitive to drug actions and are more likely to have adverse drug reactions to *anticholinergics*. The resulting *side effects* are blurred vision, confusion, disorientation, dry mouth, dry eyes, constipation, palpitations, worsening of glaucoma, and urinary retention. Males with prostate problems are at extreme risk for acute urinary retention.

Drugs that produce significant anticholinergic effects include:

- Antipsychotic agents, such as the phenothiazines, chlorpromazine, fluphenazine, thioridazine, and perphenazine
- Antidepressants, such as the tricyclics amitriptyline, doxepin, imipramine (Tofranil), and nortriptyline (Pamelor)
- Antiparkinson agents, such as benztropine (Cogentin) and trihexyphenidyl
- Antispasmodics, such as dicyclomine (Bentyl) and hyoscyamine (Levsin)
- Antihistamines, such as diphenhydramine (Benadryl) and promethazine (Phenergan)

There are many other classes of medications (SSRIs, some atypical antipsychotics, H_2 blockers, certain cardiovascular drugs, corticosteroids, etc.) that exhibit subtle anticholinergic activity that becomes more pronounced in the older adults. Because the increase in the amount of a drug circulating in the system is often gradual, the consequences of an "overdose" may not be recognized. Family, friends, and even patients themselves may conclude that their symptoms are just because of aging.

Cognitive Impairment

Many medications can cause mental health concerns in older people. One government study found that more than 150,000 older adults had experienced *serious mental impairment either caused or worsened by drugs.* Many medications can have central nervous system (CNS) *side effects,* such as anxiety, depression, confusion, disorientation, forgetfulness, hallucinations, nightmares, or impaired mental clarity, *especially in older adults.* Some drugs (this is a representative list) that can cause **mental impairment** (including dementia and delirium) in older adults include:

- Anticholinergics
- Antidepressants, tricyclic (TCAs)
- Antipsychotics (chronic and as-needed use)
- Benzodiazepines
- Corticosteroids
- H_2 receptor antagonists
- Meperidine
- Phenothiazines
- Sedative hypnotics

Avoid taking antipsychotics for behavioral challenges with dementia unless nonpharmacologic options have failed and the patient is a threat to themself or others. Antipsychotics are associated with an increased risk of cerebrovascular accidents and mortality in persons with dementia. In addition, all antipsychotics can cause tardive dyskinesia and/or parkinsonism. When discontinuing many of the listed categories of drugs used chronically, *taper to avoid withdrawal symptoms.*

Syncope/Falls

Syncope (fainting or passing out) in older adults can be attributed to age-related physiological changes in conjunction with medications that result in decreased delivery of cerebral oxygen. Many CNS and antihypertensive drugs cause dizziness or **motor impairment**, which increase the risk of falls. These drugs can also impair sexual functioning, reducing the quality of life for some older adults. Some drugs causing or contributing to syncope or falls include:

- Anticonvulsants (avoid except for treating seizures)
- Antidepressants (SSRIs and TCAs)
- Antipsychotics (especially chlorpromazine, thioridazine, and olanzapine, which increase the risk of orthostatic hypotension)

- Alpha blockers (doxazosin, prazosin, and terazosin, which increase the risk of orthostatic hypotension and tachycardia)
- Benzodiazepines
- Nonbenzodiazepine hypnotics (e.g., Ambien)

Gastrointestinal Conditions

Many older people experience chronic and acute pain and take over-the-counter (OTC) nonsteroidal anti-inflammatory drugs (NSAIDs), frequently without adequate supervision. Anyone taking NSAIDs should be cautioned about the real danger of serious complications. Every year there are over 70,000 hospitalizations and more than 7,000 deaths from drug-induced bleeding ulcers or perforations. Particularly in older adults, there may be no warning signs of pain, and the first symptom of trouble may be a "silent" bleed that could lead to fatal GI hemorrhage.

The COX-2 selective NSAID Celebrex has less *potential* for gastric problems, GI bleeding, or other bleeding problems than the other nonselective NSAIDs. However, more data is needed to confirm this. The use of PPIs and misoprostol (Cytotec) reduces but does not eliminate the risk of GI bleeding associated with NSAIDs. The key to avoiding problems with NSAIDs is to use the lowest effective dose for the shortest period of time. Consideration should also be given to a trial of acetaminophen in place of NSAIDs.

Other GI problems, for example, indigestion, heartburn, and constipation, are frequent complaints of older adults. Consequently, a common practice is the taking of OTC remedies without adequate awareness of potential side effects or implications. Side effects of antacids include constipation (with aluminum or calcium carbonate products); diarrhea (with magnesium antacids); and acid rebound, belching, or flatulence (with calcium carbonate). Avoid prolonged use (no longer than 2 weeks) of OTC antacids without medical supervision because of the danger of masking symptoms of GI bleeding or GI malignancy.

Constipation can be worsened by anticholinergics and oral antimuscarinics (e.g., oxybutynin, tolterodine) for urinary incontinence. Consider alternatives if constipation develops and avoid frequent use of strong cathartics, which can lead to laxative dependence and loss of normal bowel function. Instead, increase fluids and encourage a high-fiber diet and regular bowel habits. If laxatives are necessary, use bulk laxatives (e.g., psyllium), stool softeners, or sennosides (Senokot) or PEG 3350 (Miralax).

Cardiovascular Disease

Studies have indicated an *increased risk of cardiovascular problems* (thrombotic events, myocardial infarction [MI], and stroke) with the use of NSAIDs and COX-2 inhibitors. Consultation with the physician should include consideration of whether the benefits outweigh the potential risks.

Older adult patients with heart failure should avoid the calcium channel blockers diltiazem and verapamil, the antidiabetic glitazones (Actos, Avandia), cilostazol (Pletal), and dronedarone (Multaq). These agents have the potential to promote fluid retention and/or exacerbate heart failure.

Patient Education

Patients receiving NSAID therapy should be instructed regarding:

- Administering the medication with food
- Not exceeding the dosage prescribed by the physician
- Not taking aspirin, alcohol, or any other drugs at the same time because they may potentiate GI or bleeding problems
- The possibility of "silent" bleeding
- Reducing the dosage of NSAIDs and substituting acetaminophen for pain, if possible, at least part of the time
- Trying exercise and heat for pain control, as approved by the physician

Polypharmacy

Individuals at any age, but especially older adults, may experience **polypharmacy**, that is, the use of multiple drugs, whether they be OTC, herbals, or prescription, given at one time for the treatment of their medical conditions (Figure 27-1). The fact that a patient is on multiple medications to treat multiple medical conditions may not necessarily be problematic.

Figure 27-1 Polypharmacy: "My white pills are from my cardiologist and should be taken twice a day, my yellow pills are from my gastroenterologist for my stomach condition when needed, the pink pills are from my primary care physician for blood pressure and need to be taken in the morning . . ." In addition, many older adults add OTC medications and herbal and mineral supplements that can increase drug interactions and adverse effects.

Pinkcandy/Shutterstock.com.

Polypharmacy becomes problematic when negative outcomes occur. Polypharmacy may result in unnecessary and/or inappropriate medication prescribing, an increase in the risk of dangerous interactions with potentially serious adverse side effects, and medication nonadherence. Health care professionals should take every opportunity to educate their patients regarding their medicines, the purpose for them, possible side effects, potential dangers, and interactions between medicines. Anyone receiving medicines should be monitored on an ongoing basis to determine the continuing effectiveness and possible cumulative or adverse effects. Medicines should be reviewed regularly to determine the feasibility of reducing dosage, possibly substituting a more effective or safer medicine or discontinuing some of the medicines.

To combat polypharmacy and the adverse effects that can result from it, medication therapy management (MTM) and comprehensive medication reviews (CMRs) are becoming common practice in pharmacies. Often, insurance providers for older adult patients will provide compensation for these services to help ensure safe and effective treatment of all disease states. **Medication therapy management (MTM)** involves reviewing all a patient's medications, identifying potential or actual adverse effects or other medication-related problems, and developing a plan to optimize therapy. Often, at the end of an MTM session, the patient will be provided with a **comprehensive medication review (CMR)**, which is a document that lists their medications, how they are to take each one, and what condition they are taking each for.

All health care professionals must be aware of their responsibilities in preventing complications of drug therapy in patients of any age, but especially in older adults and the very young, who are more vulnerable. The following guidelines should be helpful:

- Health care providers should educate themselves, their patients, and their patients' families regarding adverse side effects, cumulative effects, and interactions. For example, have the American Geriatrics Society *Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults* readily available for quick reference.
- With each newly prescribed drug, note diagnoses, allergies, and other medications.

Patient Education

Older adult patients should be instructed regarding:

Making a list of *all* medications (with dosage), including pain medication, eye drops, OTC medications, vitamins and herbal remedies, and topical medications (this list should be carried in the wallet or be otherwise readily available at all times)

The purpose for their medications, side effects, the best time to take each medication, and interactions

Asking the pharmacist for easy-to-hold and easy-to-open medication containers; proper storage and importance of keeping these types of containers out of children's sight and reach

Reporting side effects to the physician immediately

The importance of visiting their physician on a regular basis, every 6 months to a year or more often, to reevaluate the need for and effectiveness of the drug

Not stopping the medicine or changing the dose without consulting the physician (abrupt withdrawal can be dangerous with some medicines)

Asking the physician to prescribe a generic or less expensive alternative if the cost of the medication is prohibitive; sometimes social service departments can assist the patient in securing expensive medications that are imperative to the patient's health; also, some drug companies will help with costs for extremely necessary expensive medications that patients cannot afford—suggest that the patient ask the pharmacist about this possibility

Asking the pharmacist to recommend a pillbox organizer or other memory aids if the patient requires help with remembering to take medications

Not taking another person's medication even if they think it is the same as theirs

Being sure all parties are informed of any issues if the patient uses one or more physicians or pharmacies

- Monitor long-term drug use for effectiveness, potential for discontinuation, and physiological or mental changes. Do periodic laboratory tests as appropriate (e.g., digoxin levels).
- *Question* any inappropriate medicine or dosage. You have a moral, ethical, and legal responsibility to do what is best for the patient.
- Document all adverse side effects, calls to the physician, and action taken.

Issues with Adherence

Nonadherence is defined as not taking medications as prescribed on a regular basis. This can result for many reasons, including side effects to a drug, lack of knowledge on how to take it, lack of understanding about why it is important, forgetfulness, decreased cognitive function, and many others. Older adult patients are often the most likely to be nonadherent, and this can result in suboptimal therapy and worsening of disease states. The best way to combat nonadherence is to first identify the reason. In some cases, patient education or reinforcement is sufficient. In particular, older adult patients are often given weekly pill boxes (Figure 27-2), unit dose packs, or pill box alarms that can help aid those who are forgetful or have decreased cognitive function. Additionally, a caregiver can help to increase overall patient adherence and can help report other reasons for nonadherence such as a side effect.

SAT MORN
FRI MORN
THUR MORN
SAT NOON
FRI NOON
THUR NOON
WED NOON
SAT EVE
FRI EVE
THUR EVE
WED EVE
SAT BED
FRI BED
THUR BED
WED BED
TUES BED
THU
WED
FRI
SAT
SUN

Razmarinka/Shutterstock.com.

eurobanks/Shutterstock.com.

Figure 27-2 Pill boxes can help older adult patients remember to take medications.

Pediatric Considerations

There are some factors for infants and pediatric patients that must be taken into consideration when prescribing medications that are primarily intended for adults. Small children have not only decreased body surface area and volume, their physiology also differs from adult patients. Some medications are researched and developed specifically for childhood use and for diseases that affect children primarily. These drugs are intended for pediatric use and their dosing is intended for children. Yet, many drugs used in the younger patient age group are not studied in children because they are underrepresented in studies. Therefore, it is important that pediatric clinicians take special care when using medications intended for adults.

Pediatric patients are generally classified into five main age groups. These age groups are important to be aware of because dosing ranges are often broken down by either age or weight. Although there is some variance, these are the generally agreed-upon groups:

- Neonates—birth to 28 days (the first 4 weeks)
- Infants—29 days to 12 months (1 year)
- Children—1 year to 12 years
- Adolescents—13 to 17 years
- Young Adults—18 to 24 years

After this, patients are considered "adults," and continue to be considered so until they are reclassified as older adults.

As you would expect, many times children receive lower doses than adults when given the same medication. There are multiple ways to calculate correct dosing for children, but these formulas are based on age, weight, and/or other factors.

Some medications intended for adult use have been formulated specifically for children in either alternative doses or formulations. Many times, children have difficulty swallowing pills, especially larger ones. To help avoid these issues, many oral tablets and capsules have been reformulated by drug companies and are available in chewable tablets, sprinkle capsules, suspensions, or solutions (Figure 27-3).

Yakobchuk Viacheslav/Shutterstock.com.

Figure 27-3 Children require alternative drug formulations if they cannot swallow.

Sprinkle capsules can be opened by the parent or caregiver and sprinkled over a tablespoon of cold or lukewarm soft food, such as pudding or applesauce. The other formulations are designed to include an appealing flavor, so they are more easily tolerated by children. Even so, sometimes children will spit up or spit out liquid medication formulations or not swallow all of a chewable tablet due to its chalky texture. It is important to instruct parents to provide a full dose, and clinicians should prescribe extra medication if replacement doses are used. Refer to Figure 27-4.

Donald R. Swartz/Shutterstock.com.

Figure 27-4 Chewable tablets are often flavored to encourage children's compliance.

Clinical Connection

Does My Calculation Make Sense?

When performing calculations for dosing adjustments, for children or any other reason, it is always important to stop and ask yourself "Does this make sense?" Many drug dose calculation errors can be identified by asking this simple question. When calculating childhood dosing, you may be asked to use a conversion rate expressed in milligrams per kilogram (mg/kg). This is interpreted as "mg of drug" per "kilogram of bodyweight." So, for example, drug A is given to adults at a dose of 10 mg daily. If drug A is prescribed for an 8-year-old child at 0.2 mg/kg per dose and the child weighs 25 kg, you can calculate the dose:

$$25\text{ kg}\left(\frac{0.2\text{ mg}}{1\text{ kg}}\right) = 5\text{ mg}$$

so the dose would be 5 mg per dose. Taking an extra minute to compare your calculation allows you to realize that an 8-year-old child taking half the dose used for an adult makes sense. On the other hand, if you had done the calculation incorrectly,

$$25\text{ kg}\left(\frac{1\text{ Kg}}{0.2\text{ mg}}\right) = 125\text{ mg}$$

and had gotten 125 mg as the dose, you should realize a child should not be receiving a dose 12.5 times higher than that of an adult. Taking an extra second to ask this question after performing any calculation can help avoid drug errors, but special care should be taken when adjusting for children.

Body Composition

The ADME processes for children can vary greatly from that of an adult and if not accounted for can lead to potential side effects or dangerous overdose. Additionally, as children age, their physiology changes and becomes closer to that of an adult. To account for this, clinicians must constantly be ready to adjust treatment or dosing as children grow.

Absorption: Similar to older adults, infants and children have a lower gastrointestinal pH and slower motility in the bowels. Additionally, they have a shorter GI tract and faster gastric emptying rate that can also decrease absorption. For medications that affect the bowels locally or are absorbed in the gut, dosing adjustments may need to be made.

Distribution: A much higher percentage of the body mass of infants and children is made up of water, so drugs that are water soluble may require higher doses. Conversely, their fat content is low compared to that of average adults, so medications that are fat soluble may require dose adjustments. This volume of distribution changes throughout the child's early life and needs to be accounted for when a child is on a maintenance medication. Protein binding to drugs is also decreased in this population because of decreased albumin levels. In this case, doses would need to be decreased, or overdose of unbound (free) medication levels in the blood could occur.

Metabolism: In general, drug metabolism via the liver in infants and children is lower than that of adults. Although it can fluctuate throughout early life, it does not reach the same level until after the child is an adolescent. Drugs metabolized primarily by the liver should be used in lower doses. One such example is acetaminophen. Childhood dosing is much lower (one-half to one-quarter of the dose used by adults) and can cause serious side effects if not done correctly.

Excretion: In the early stages of life glomerular filtration rate (GFR), renal blood flow, and tubular secretion are all decreased, which means drugs can stay in the body longer and have the potential to accumulate and therefore should be used at lower doses if they are primarily excreted via the kidneys. Although you will not be expected to know specific doses for children, it is important to be aware of these considerations as a health care professional.

Understanding that pediatric patients may require special medication considerations is half the battle. Although you will not be required to know all the specific details, it is important to realize that patients in this age group are not adults, and decisions regarding their medication and treatment should be adjusted accordingly.

Case Study A

Drugs and Older Adults

A grandchild is concerned that a grandparent is not taking their medications correctly. The patient is on phenytoin, theophylline, digoxin, and a benzodiazepine.

1. What is the most likely age-related effect of the medications taken by the patient?
- a. High risk for periodic severe hypoglycemia
- b. Frequent changes in the dose and schedule of her medications
- c. Slowed clearance of drugs from her system, resulting in potentially cumulative effects
- d. Increased clearance of drugs, resulting in the need for higher doses of the medication

2. How do benzodiazepines affect older adults as opposed to younger adults?
- a. Older adults have a decreased sensitivity to the drug.
- b. Older adults have largely the same reaction to the drug as young adults.
- c. Older adults require an increased dosage of the drug.
- d. Older adults have an increased sensitivity to the drug.

3. What is the best method for monitoring phenytoin therapy?
- a. 24-h urine check
- b. Patient reports of seizure activity
- c. Serum phenytoin level
- d. EEG

4. Consider that water accounts for only 45% of an older adult's body weight. How will this most likely affect the patient's physiological response to theophylline?
- a. The patient may need a larger dose.
- b. The patient's vital signs may be critically affected.
- c. The patient's response will not be affected by this.
- d. The patient may need a smaller dose.

5. The patient has just been diagnosed with reduced renal function. What category of drugs may be particularly dangerous to add to their drug list?
- a. Aminoglycosides
- b. Antihistamines
- c. Salicylates
- d. Calcium channel blockers

Case Study B

Drugs and Older Adults

A nurse visits an older adult patient who is living independently in a small apartment. During the intake interview, the nurse asks the patient about their medical history and their current medications. The patient reports their history to the nurse and then retrieves a large brown paper bag from the kitchen with numerous medications, explaining that they take all the medications in the bag.

1. Polypharmacy is the use of medication and is more specifically defined as:
- a. Applying to prescription drugs only
- b. Taking two drugs at a time
- c. Taking one drug for at least 14 days
- d. The use of multiple drugs, either OTC or prescription

2. The nurse should instruct the patient, at a minimum, to keep a list of which medications?
- a. Only prescription drugs
- b. Prescription drugs and OTC drugs
- c. Prescription drugs, OTC drugs, and vitamins
- d. Prescription drugs, OTC drugs, vitamins, and herbal or mineral supplements

(*Continued*)

3. The nurse decides to set up a system for the patient. What method will be most beneficial to help the patient take the correct pills on the correct days?

a. A note on their bathroom mirror
b. A daily pillbox organizer
c. A mailed reminder card from their primary care physician
d. A monthly phone call reminder from the local pharmacy

4. The nurse decides to give the patient further instructions regarding their medications. Which item should be included in the teaching plan?

a. In case of a missed dose, take two pills at the next scheduled dose.
b. Memorize the purpose of each medication.
c. Keep an updated list of all medications, including dose and frequency, in your wallet.
d. Always request a generic medication when filling a prescription.

5. When the nurse is reviewing the patient's medications, they are following a moral, ethical, and legal responsibility when they:

a. Question an inappropriate medication and/or dose
b. Disregard the patient's concerns about a particular medication
c. Discard pills that the patient did not take
d. Change the dose of a medication to better address the patient's symptoms

Note

A Comprehensive Review Exam for Part II can be found at the end of the text following the Summary.

Chapter Review Quiz

Choose the correct answer. Please note that some questions require you to refer to the updated Beer's criteria for PIM use in older adults.

1. The aging process is:

a. The same in individuals in similar decades of life
b. Very individualized
c. Different based upon ethnicity
d. Slowed in males versus females

2. As an individual age, the gastric pH:

a. Stays at the same level
b. Fluctuates over time
c. Increases
d. Decreases

3. You are educating an older adult who is taking a quinolone antibiotic in conjunction with an antacid. When should the patient be instructed to take the quinolone as it relates to the antacid?

a. Take with the antacid.
b. Take 1 h prior to the antacid.
c. Take 1 h post antacid.
d. Do not take within 2 h of antacid.

4. Cumulative effects of drugs in older adults can be because of:

a. Increased GI motility

b. Higher metabolism

c. Inadequate absorption

d. Improved renal function

5. What is an example of an antipsychotic drug that produces significant anticholinergic effects in older adults?

a. amitriptyline

b. benztropine

c. chlorpromazine

d. diphenhydramine

6. Which of these is an appropriate medication for treating arthritis pain in older adults?

a. Indocin

b. Ketorolac

c. Acetaminophen

d. Talwin

7. Which of these is an appropriate medication for treating allergies in older adults?

a. Benadryl

b. Claritin

c. Chlor-Trimeton

d. Vistaril

8. Which of these is an appropriate pain medication for older adults after surgery?

a. Morphine

b. Indocin

c. Demerol

d. Talwin

9. When starting an older adult patient on a new drug, which is the best method of dosing?

a. Allow the patient to titrate the dose to the desired effect

b. Start with a high dose and then reduce to the desired effect

c. Start with a moderate dose for the least risk with the most effectiveness

d. Start at the lowest effective dose and increase slowly to avoid adverse effects

10. Which category of drugs is most likely to cause dizziness or motor impairment, increase the risk of falls, and impact sexual functioning in older adults?

a. Anticoagulants

b. Antihypertensives

c. Anti-infectives

d. Antidiabetics

11. Which of these cardiac drugs is *least* appropriate for older adults?

a. Norpace

b. Vasotec

c. Procardia XL

d. Hydralazine

12. Which one of these is an appropriate antidepressant for treating older adults with no history of seizure disorder?

a. Prozac

b. amitriptyline

c. doxepin

d. Wellbutrin

13. Which organ's function decreases with age, resulting in a decline of creatinine clearance?

a. Liver
b. Kidney
c. Small intestine
d. Large intestine

14. Which two categories of drug therapy are responsible for more than two-thirds of drug-related hospitalizations in older adult patients?

a. Antidiabetic/antithrombotic
b. Antihypertensive/anticoagulants
c. Antidiabetic/antihypertensive
d. Antidepressant/antihypertensive

15. Older adults are very sensitive to drug actions and are more likely to have adverse reactions to anticholinergics. What is a potential side effect of an anticholinergic?

a. Drooling
b. Constipation
c. Urinary frequency
d. Diarrhea

16. Which of the following is *not* an alternative formulation used for younger patients who have trouble swallowing?

a. Liquids
b. Chewable tablet
c. Sprinkle capsule
d. Orally disintegrating tablet

17. The bodies of younger patients have a higher percentage of water than those of adults, and this requires dosing adjustments with certain drugs.

a. True
b. False

18. What is the term for when a medication has the opposite effect on a patient or group of patients (such as young children) compared to the average adult?

a. Symbiotic reaction
b. Paradoxical effect
c. ADME process
d. Syncope

Summary

The health care professional has a great responsibility in both the administration of medications and advising patients regarding drug therapy. As the older adult population increases, many new drugs are being developed and prescribed, requiring knowledge regarding their cumulative effects and interactions. The moral, ethical, and legal issues of drug therapy are being raised with increasing frequency. Therefore, it is imperative that the health care professional keep informed of changes in drug therapy practices. Complete knowledge and good judgment are necessary for effective administration and adequate patient education.

The following guidelines should prove useful for safe drug therapy:

- Always research new drugs before administration to determine their side effects, interactions, and cautions.
- Always verify that you are administering the drug to the correct patient by whatever system your institution utilizes. If the patient is wearing a wristband, this must always be checked.
- Assess the patient before administration for allergies, general condition, and possible contraindications and after administration for results and adverse effects.
- Question any inappropriate drugs, dosages, or possible interactions.
- Reduce the risk of medication errors by checking the spelling of each medicine very carefully. Many drug names look or sound alike, but the drugs act differently. Check the patient's diagnosis to be sure the medication is appropriate.

Comprehensive Exam For Part 1

Choose one correct answer and mark the appropriate letter.

1. Drug standards regulate which factors in drug preparation?

a. strength, quality, purity
b. fillers, color, taste
c. color, taste, quality
d. quality, fillers, taste

2. The Pure Food and Drug Act

a. requires warning labels on certain medications
b. sets limitations on prescription use
c. establishes consumer protection
d. was passed in 1976

3. The Food and Drug Administration regulates

a. prescriber registration
b. creation of drug schedules
c. prescription labeling
d. establishment of drug regulations

4. Controlled substances include

a. Digoxin and Tylenol
b. Benadryl and Cardizem
c. Ampicillin and ibuprofen
d. Valium and oxycodone

5. Controlled drugs

a. are listed by schedule
b. have no limitations on refills
c. do not cause dependence
d. are available over the counter

6. A good source of drug information is

a. news magazines
b. your colleagues
c. social networks
d. *PDR*

7. The generic name of a drug is

a. assigned by the drug company
b. written in capital letters
c. the common name
d. the same as the trade name

8. The term *OTC* refers to drugs that

a. are often controlled
b. require a prescription
c. are sold over the counter
d. are officially certified

9. Two conditions commonly listed as *contraindications* for drug administration are

a. obesity and glaucoma
b. hypersensitivity and pregnancy
c. psychosis and seizures
d. glaucoma and anemia

10. Before giving a new drug, you must know

a. its absorption rate
b. the distribution process it will follow
c. its excretion rate
d. its indication for use and side effects

11. An antibiotic with *photosensitivity* listed as a side effect could cause

a. deafness
b. sunburn
c. blindness
d. kidney damage

12. The initial high dose to quickly elevate drug levels is the

a. loading dose
b. maintenance dose
c. maximum dose
d. therapeutic dose

13. An accumulation of a normal drug dosage can best be explained by what pharmacokinetic change?

a. increase in metabolism
b. increase in excretion
c. decrease in metabolism
d. decrease in absorption

14. Patient characteristics affect the processing of drugs in the body. Two of these characteristics are

a. hair color and gender
b. skin color and mental status
c. income and age
d. weight and age

15. Drug toxicity from cumulative effects may result from

a. intracranial pressure
b. glaucoma
c. kidney malfunction
d. high blood pressure

16. Idiosyncrasy means

a. an opposite effect from that expected
b. an allergic response to a drug
c. a unique, unusual, and unexpected response to a drug
d. having an effect from a drug as the result of suggestion

17. The route of administration most often used is

a. topical
b. sublingual
c. injection
d. oral

18. A form of parenteral administration is

a. nasogastric tube
b. injection
c. oral
d. rectal

19. A type of medication that can be crushed and mixed with food to facilitate administration is

a. time-release capsule
b. lozenge
c. capsule
d. enteric-coated tablet

20. Topical administration includes which of the following?

a. nebulizer
b. cream
c. sublingual
d. inhalation

21. The most rapid form of administration is

a. PO
b. IV
c. IM
d. SQ

22. The least accurate system for measuring medication is

a. metric
b. apothecary
c. household
d. standard

23. The most frequently used system for measuring medicine is

a. apothecary
b. metric
c. household
d. standard

24. Medication orders must contain

a. patient's address
b. alternate drugs
c. physician's address
d. drug name, dosage, and route

25. The prescription blank for a controlled substance must contain

a. name of the drug company
b. physician's DEA number
c. physician's address
d. lot number of the drug

26. The least accurate type of equipment for measuring medicine is a

a. medicine cup
b. calibrated utensil
c. tablespoon
d. syringe

27. Responsibilities of the health care professional in drug administration include

a. assessing and evaluating patients
b. checking the order for accuracy
c. reporting adverse patient outcomes
d. all of the above

28. After administering medication, you should

a. inform the patient's family
b. document drugs administered
c. complete additional treatments ordered
d. administer drugs to the next patient

29. The most helpful patient information to know when administering medication is

a. patient's residence
b. patient's disabilities
c. patient's health history, including allergies
d. patient's occupation

30. If a medication error is made, once the patient is cared for you should

a. immediately report the error to the physician
b. file an incident report
c. note the error on the patient record
d. apologize to the patient

31. Before giving any medicine, it is essential to review the Rights of Medication Administration, including

a. right medication and right amount
b. right physician and DEA number
c. right drug company
d. right drug lot

32. Documentation of a controlled drug given PRN for pain requires

a. review of pharmacy delivery record
b. re-evaluation of effectiveness
c. note of the trade name
d. review of the physician's comments

33. Administration by the gastrointestinal route includes which of the following?

a. PEG tube
b. oral inhaler
c. transdermal patch
d. eye drops

34. An advantage of the oral route over other routes is that it

a. absorbs the most quickly
b. is the best route to treat emergencies
c. is economical, with few equipment costs
d. can be used for all patients all the time

35. If a medication is ordered PO and the patient has an NPO order, you should

a. give the medication by injection
b. give the medication rectally
c. omit the medication and note on the chart
d. consult the person who ordered the medication

36. Oral medications are usually best administered with

a. fruit juice
b. milk
c. water
d. hot tea

37. When preparing the proper dosage of cough syrup, you should

a. shake the bottle
b. dilute with liquid
c. hold the bottle with the label side down
d. hold the medicine cup at eye level

38. When administering a rectal suppository, you should

a. assist the patient to self-administer
b. provide privacy and use disposable gloves
c. turn the patient onto the right side
d. warm the suppository under warm water

39. The parenteral route *least* likely to be used for systemic effects is

a. transdermal
b. topical
c. sublingual
d. inhalation

40. The route with the slowest action is

a. transcutaneous
b. inhalation
c. sublingual
d. injection

41. After instilling eye drops, you should

a. rub the eyelid vigorously
b. press on the inner canthus
c. close the eyelid quickly
d. discard the eyedropper

42. For intradermal injection, you should

a. use a tuberculin syringe
b. use a 21-gauge, 1-inch needle
c. pinch the skin
d. inject 1–3 mL of solution

43. Which of the following is not true for intramuscular injections?

a. pinch the skin
b. administer at a 45-degree angle of needle
c. use a 1½-inch needle for most patients
d. always administer Z-track for medications that are irritating to tissue

44. Which of the following IM injection sites is most commonly used for adult immunizations?

a. dorsogluteal
b. vastus lateralis
c. ventrogluteal
d. deltoid

45. Before administering medication via NG tube, you should verify placement by

a. injecting 10 mL water
b. attaching NG to suction
c. having an X-ray of the abdomen taken
d. checking the pH of gastric aspirate

46. If a 2-year-old accidentally swallows several children's aspirin tablets, you should

a. administer ipecac
b. give activated charcoal
c. call Poison Control
d. give 8 oz of milk

47. If there is doubt about the type of poison ingested by an individual, toxicology tests will be done on body fluids, including

a. tears and saliva
b. blood and urine
c. stool and emesis
d. emesis and tears

48. The groups at greatest risk of accidental poisoning are

a. young children and older adults
b. adolescents and healthy adults
c. healthy adults and adults with disabilities
d. adolescents and dementia patients

49. Prevention is the key to preventing harm and death from poisoning. The key to prevention is

a. legislation
b. oversight
c. regulation
d. public education

50. For which of the following is the IV route used?

a. correct body fluid imbalances
b. administer blood
c. administer medications
d. all of the above

51. How many types of IV administration are there?

a. one
b. two
c. three
d. four

52. Which of the following is an isotonic fluid?

a. lactated Ringers
b. ½ NSS
c. D5W
d. D5LR

53. A self-administered inhalational device that utilizes a propellant to deliver the medication is a(an)

a. DPI
b. SVN
c. MDI
d. PEG

54. Who discovered penicillin?

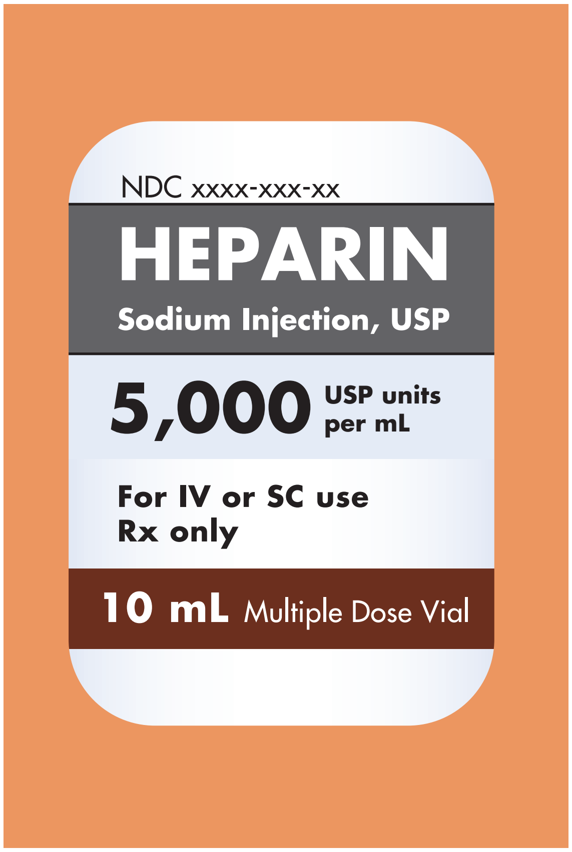
a. Alexander Fleming
b. Oswald Schmeideberg
c. Alfred Einhorn
d. Watson and Crick

55. Why is Tall Man Lettering used?

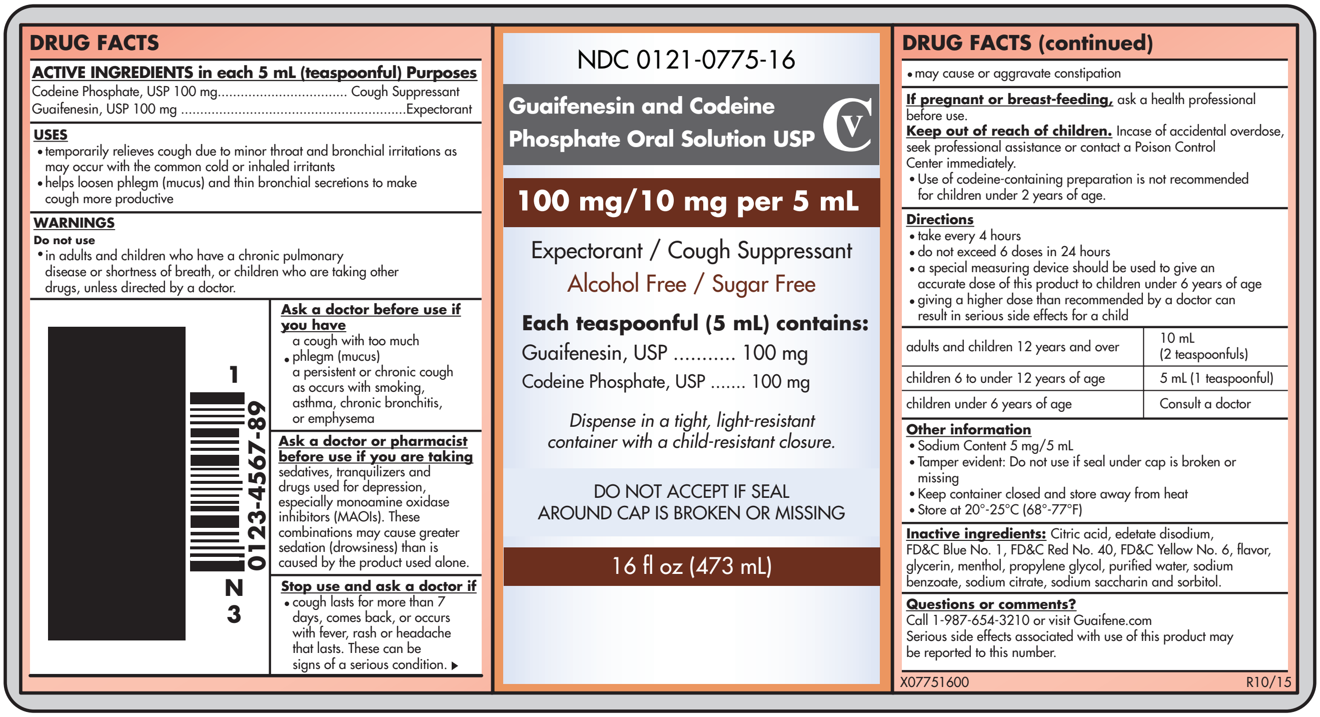
a. It looks appealing to customers.
b. It highlights differences in sound-alike medications.
c. It adds confusion.
d. It helps patients spell the drug names.

Calculate the correct dosage for administration in the following problems. Label your answers. Remember that syringes are not marked in fractions; therefore, when computing dosages for administration, you must convert all fractions to decimals and round off to one decimal place.

56. You are to give 7,500 units of heparin SQ. How many milliliters should you give?


NDC xxxx-xxx-xx
HEPARIN
Sodium Injection, USP
5,000 USP units per mL
For IV or SC use
Rx only
10 mL Multiple Dose Vial

57. You are to give 10 mL of guaifenesin cough syrup with codeine. How much codeine would the patient receive in each prescribed dose?



DRUG FACTS

ACTIVE INGREDIENTS in each 5 mL (teaspoonful) Purposes

Codeine Phosphate, USP 100 mg.................................. Cough Suppressant
Guaifenesin, USP 100 mg ....Expectorant

USES

- temporarily relieves cough due to minor throat and bronchial irritations as may occur with the common cold or inhaled irritants
- helps loosen phlegm (mucus) and thin bronchial secretions to make cough more productive

WARNINGS

Do not use

- in adults and children who have a chronic pulmonary disease or shortness of breath, or children who are taking other drugs, unless directed by a doctor.

N 3 0123-4567-89 1

Ask a doctor before use if you have

- a cough with too much phlegm (mucus) a persistent or chronic cough as occurs with smoking, asthma, chronic bronchitis, or emphysema

Ask a doctor or pharmacist before use if you are taking sedatives, tranquilizers and drugs used for depression, especially monoamine oxidase inhibitors (MAOIs). These combinations may cause greater sedation (drowsiness) than is caused by the product used alone.

Stop use and ask a doctor if

- cough lasts for more than 7 days, comes back, or occurs with fever, rash or headache that lasts. These can be signs of a serious condition. ▶

NDC 0121-0775-16

Guaifenesin and Codeine Phosphate Oral Solution USP CV

100 mg/10 mg per 5 mL

Expectorant / Cough Suppressant
Alcohol Free / Sugar Free

Each teaspoonful (5 mL) contains:
Guaifenesin, USP .... 100 mg
Codeine Phosphate, USP .... 100 mg

Dispense in a tight, light-resistant container with a child-resistant closure.

DO NOT ACCEPT IF SEAL AROUND CAP IS BROKEN OR MISSING

16 fl oz (473 mL)

DRUG FACTS (continued)

- may cause or aggravate constipation

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children. Incase of accidental overdose, seek professional assistance or contact a Poison Control Center immediately.

- Use of codeine-containing preparation is not recommended for children under 2 years of age.

Directions

- take every 4 hours
- do not exceed 6 doses in 24 hours
- a special measuring device should be used to give an accurate dose of this product to children under 6 years of age
- giving a higher dose than recommended by a doctor can result in serious side effects for a child

adults and children 12 years and over	10 mL (2 teaspoonfuls)
children 6 to under 12 years of age	5 mL (1 teaspoonful)
children under 6 years of age	Consult a doctor

Other information

- Sodium Content 5 mg/5 mL
- Tamper evident: Do not use if seal under cap is broken or missing
- Keep container closed and store away from heat
- Store at 20°-25°C (68°-77°F)

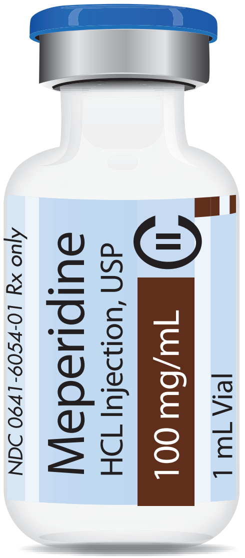
Inactive ingredients: Citric acid, edetate disodium, FD&C Blue No. 1, FD&C Red No. 40, FD&C Yellow No. 6, flavor, glycerin, menthol, propylene glycol, purified water, sodium benzoate, sodium citrate, sodium saccharin and sorbitol.

Questions or comments?
Call 1-987-654-3210 or visit Guaifene.com
Serious side effects associated with use of this product may be reported to this number.

X07751600 R10/15

58. The medicine bottle label states that the strength of each tablet in the bottle is 0.25 mg. The physician has ordered that the patient is to receive 0.5 mg. How many tablets should you give?

59. The physician has ordered 50 mg of meperidine to be given. How many milliliters should you give?



60. To convert pounds to kilograms (kg), you would divide the number of pounds by what number?

Comprehensive Exam For Part 2

Choose one correct answer and mark the appropriate letter.

1. Vitamin C aids in the absorption of
   a. protein
   b. iron
   c. fat
   d. zinc

2. What is one side effect of taking an iron preparation?
   a. blood-tinged stools
   b. brown stools
   c. white stools
   d. black stools

3. Which vaccine is recommended for all persons over the age of 50 years?
   a. Gardasil-9
   b. Adacel
   c. Prevnar 20
   d. Shingrix

4. Which side effect may occur after prolonged use of a corticosteroid cream?
   a. hyperglycemia
   b. epidermal thinning with frequent skin tears
   c. immunodeficiency disorders
   d. systemic viral infection

5. Which type of preparation is used topically to soothe the skin and seal out wetness from diaper rash?
   a. keratolytics
   b. antipruritics
   c. protectants
   d. enzymatics

6. A yeast infection of the tongue is medically known as
   a. tinea pedis
   b. varicella zoster
   c. tinea coporis
   d. candidiasis

7. A common topical antifungal medication used for athlete's foot would be
   a. clotrimazole
   b. betamethasone
   c. mupirocin
   d. povidone–iodine

8. Drugs that mimic the action of the sympathetic nervous system are known as
   a. adrenergics
   b. cardiogenics
   c. adrenergic blockers
   d. cholinergics

9. Adrenergics should be used with caution in patients with
   a. hypotension
   b. angina
   c. asthma
   d. diabetes

10. Cholinergic blockers would most likely cause which of the following side effects?
   a. hypotension
   b. photosensitivity
   c. dry mouth and constipation
   d. enhanced vision

11. What would be the best food choice for an individual undergoing treatment with an antineoplastic?
   a. spaghetti and meatballs
   b. orange juice
   c. mashed potatoes
   d. peppered steak

12. A clinician is reviewing an order sheet for a patient with breast cancer. Herceptin is ordered to be given orally. The clinician knows that this is an error and that instead the drug should be administered by which route?

a. intrathecal
b. intravenous
c. topical
d. intramuscular injection

13. Plant alkaloids can be fatal if administered by which route?

a. intrathecal
b. intravenous
c. oral
d. intraosseous

14. The main indication for the use of a diuretic is to

a. reduce bladder spasm
b. promote excretion of uric acid
c. reduce urinary frequency
d. reduce the circulating fluid volume

15. Which of the following is a common side effect of all the antineoplastic agents discussed?

a. photosensitivity
b. cardiotoxicity
c. GI effects such as nausea and vomiting
d. extravasation

16. What condition is medical marijuana not used to treat (in states that allow it)?

a. end-of-life situations where palliative care is a priority (pain)
b. PTSD/depression
c. anxiety
d. dizziness

17. UTIs are commonly treated with

a. antibiotics and Pyridium
b. steroids and fluids
c. antibiotics and ibuprofen
d. nothing; uncomplicated UTIs self-resolve

18. Long-term use of agents that reduce gastric acid can possibly result in a deficiency of which vitamin?

a. vitamin D
b. vitamin E
c. vitamin C
d. vitamin B_{12}

19. The drug mesalamine produces an anti-inflammatory effect in which section of the gastrointestinal tract?

a. stomach
b. colon
c. esophagus
d. duodenum

20. What instruction should be given with a prescription for esomeprazole (Nexium) and other PPIs?

a. Take 2 h after a meal.
b. Take on an empty stomach.
c. Take with water only.
d. Take with meals.

21. What is the drug of choice for infective endocarditis prophylaxis?

a. penicillin
b. cefaclor
c. amikacin
d. amoxicillin

22. What is a potential hypersensitivity reaction caused by vancomycin?

a. red rash of the face and upper torso
b. lactic acidosis
c. flushing of hands
d. elevated CPK

23. Amphotericin B is administered by which route?

a. oral
b. intravenous
c. intramuscular
d. transdermal

24. What is the primary function of mydriatic eye preparations?

a. pupil constriction
b. pupil dilation
c. corneal anti-inflammatory
d. retinal anesthetic

25. Patients being treated with an anti-infective ophthalmic preparation should be instructed to

a. avoid eye makeup

b. wear contact lenses for not more than 12 h a day

c. instill into the upper eyelid area

d. use drops only until symptoms begin to improve

26. Which is a key guideline in educating a patient with an eye infection?

a. consider an eye patch as an effective alternative to an antibiotic for treatment

b. engage in careful handwashing to prevent the spread of infection

c. gently massage the upper eyelid after instillation of eye drops

d. when using more than one drop instill both drops at the same time

27. Large doses of acetaminophen can cause which side effect?

a. gastric ulcer

b. petechiae

c. liver toxicity

d. splenic swelling

28. Opioids can tend to cause tolerance, which is

a. when the drug is stopped, withdrawal symptoms occur

b. when the person has a physical need to take the drug

c. when the drug is not tolerated in the body and side effects occur

d. when a larger dose of the drug is needed to achieve the same effect

29. Why may a lidocaine patch be of benefit to a patient experiencing postherpetic neuralgia?

a. It acts peripherally with little CNS action.

b. It produces an anesthetic effect.

c. It acts as a CNS depressant.

d. It produces an anti-inflammatory effect.

30. What is the preferred first-step intervention in treating insomnia?

a. barbiturates

b. benzodiazepines

c. nondrug therapies

d. nonbenzodiazepines

31. What is a possible side effect of an overdose of a tricyclic antidepressant?

a. hypertension

b. mania

c. hyperglycemia

d. tachyarrhythmias

32. Which antidepressant can be useful in a patient with severe depression characterized by extreme fatigue, lethargy, and psychomotor retardation?

a. mirtazapine

b. bupropion

c. imipramine

d. trazodone

33. Which vital sign should be monitored continuously when administering midazolam (or any benzodiazepine) to a patient?

a. blood pressure

b. pulse

c. temperature

d. respiratory rate

34. What is first-line therapy for children with ADHD?

a. stimulants such as Adderall or Ritalin

b. antidepressants such as Celexa or Zoloft

c. nonpharmacological therapy

d. all of the above

35. The use of skeletal muscle relaxants is of greatest concern, and should be avoided, in which population?

a. young children

b. older adults

c. people who are pregnant or breastfeeding

d. individuals with bone cancer

36. Individuals with a sulfonamide hypersensitivity should follow which guideline when taking celecoxib (Celebrex)?

a. take only three doses
b. take for one month
c. avoid taking the drug
d. wait 2 h after aspirin ingestion

37. What is the IV drug of choice to treat status epilepticus?

a. diazepam
b. lorazepam
c. valproic acid
d. fosphenytoin

38. A patient taking entacapone (Comtan) may need assistance with getting out of bed due to which possible side effect?

a. muscular stiffness
b. peripheral neuropathy
c. orthostatic hypotension
d. tachycardia

39. Which anticonvulsant is considered "broad-spectrum" and is useful for the management of many seizure types?

a. phenytoin
b. oxcarbamazepine
c. valproic acid
d. clonazepam

40. Corticosteroids can be used to treat all of the following EXCEPT

a. allergic reactions
b. respiratory disorders
c. malignancies
d. headaches

41. A patient taking thyroid replacement medication (like levothyroxine) should be instructed to take it

a. anytime during the day
b. only when they are having symptoms
c. on an empty stomach in the morning
d. before bed with a snack

42. An overdosage of thyroid replacement medication (like levothyroxine) is manifested in which of the following ophthalmic conditions?

a. drooping eyelids
b. bulging eyeballs
c. dilated pupils
d. reddened conjunctive

43. Which oral medication for diabetes is considered first-line therapy?

a. metformin
b. Januvia
c. Lantus
d. Victoza

44. Which of the following is a long-acting insulin?

a. Novolog
b. Novolin N
c. Levemir
d. Apidra

45. Insulin should be injected

a. in the largest muscle every time
b. in various muscles with the patient rotating sites
c. subcutaneously with the patient rotating sites
d. subcutaneously in the back of the arm only

46. If a diabetic patient is hypoglycemic, what is a reasonable choice for acute treatment?

a. 4 oz of orange juice
b. sugar-free candy
c. a small portion of red meat
d. 8 oz of diet soda

47. What hormone is responsible for the changes in the uterine endometrium during the second half of the menstrual cycle in preparation for implantation of the fertilized ovum?

a. estrogen
b. progesterone
c. gonadotropin-releasing hormone
d. testosterone

48. What is one side effect of continuous progestin?

a. breast size reduction
b. weight loss
c. constipation
d. amenorrhea

49. Postcoital contraception should be taken within how many hours of unprotected sex?

a. 48 h
b. 24 h
c. 96 h
d. 72 h

50. Which of the following is critical to monitor prior to administering digoxin?

a. blood pressure
b. radial pulse rate
c. apical heart rate
d. respiratory rate

51. Digoxin taken in conjunction with what type of medications can increase the chance of arrhythmias?

a. antacids
b. macrolides
c. benzodiazepines
d. diuretics

52. Which antiarrhythmic may cause tachycardia?

a. procainamide
b. adenosine
c. verapamil
d. metoprolol

53. Which medication could be used to replace an ACE inhibitor when a patient has problems with a dry cough as a side effect?

a. losartan
b. metoprolol
c. digoxin
d. atorvastatin

54. The most effective and most commonly used antilipemic medications are called

a. bile acid sequestrates
b. statins
c. nicotinic acids
d. fibrates

55. Warfarin is monitored with what laboratory method?

a. complete blood work with differential
b. LH levels
c. TSH levels
d. INR

56. Clopidogrel should not be taken with which of the following medications?

a. OTC Zantac
b. OTC aspirin
c. OTC Prilosec
d. OTC Pepcid

57. In patients with COPD, what precaution should be taken when administering oxygen?

a. avoid smoking when in use
b. always use the highest concentration tolerable
c. only use a nasal cannula to delivery it
d. use for no more than 1 h continuously

58. What is the preferred route of administration of bronchodilators to minimize systemic adverse effects?

a. oral
b. injection
c. sublingual
d. inhalation

59. Which antitussive has the greatest effectiveness?

a. codeine
b. hydrocodone
c. benzonatate
d. dextromethorphan

60. What is one side effect of nicotine replacement products?

a. diarrhea
b. thickened secretions
c. hyperglycemia
d. nausea and vomiting

61. Why should older adults avoid taking over-the-counter (OTC) antacids for longer than 2 weeks without medical supervision?

a. OTC antacids may mask GI bleed.
b. OTC antacids may cause *C. difficile* infection.
c. OTC antacids may cause excessive flatulence.
d. OTC antacids may cause urinary incontinence.

62. Constipation is a concern for older adults. Which is a suggested first-line laxative for this population?

a. calcium carbonate
b. bismuth sulfate
c. magnesium citrate
d. sennosides

63. What is the key strategy to avoiding problems when taking NSAIDs?

a. take on an empty stomach
b. take in conjunction with Tylenol
c. take the lowest effective dose for the shortest time period with food or milk
d. take for no more than 28 days continuously

64. What is one potential side effect of a calcium carbonate antacid?

a. mild diuresis
b. constipation
c. diarrhea
d. nausea

65. Due to various reasons, older adult patients tend to

a. take medications exactly as prescribed
b. be nonadherent to one or more medications
c. go to one pharmacy and one doctor for all their health care needs
d. be on few medications

66. Which treatment for gout is reserved for those who have failed other therapy and is administered IV?

a. allopurinol
b. Uloric
c. Colcrys
d. Krystexxa

67. The combination medication Duexis (famotidine and ibuprofen) is supplied in combination form for what reason?

a. To increase patient adherence
b. To decrease cost of medication
c. Because ibuprofen and other NSAIDs can cause stomach ulcers, the famotidine (H_2 blocker) acts as a protectant.
d. Because famotidine and other H_2 blockers can cause stomach ulcers, the ibuprofen (NSAID) acts as a protectant.

68. When taking SSRIs or tricyclic antidepressants, within which time frame should patients expect to see symptom relief?

a. 2–6 weeks
b. 1–2 days
c. 1–3 years
d. 30–60 min

69. Which of the following is the correct representation for insulin concentration?

a. U-500 means there are 500 units of insulin per 10 mL.
b. U-100 means there are 100 units of insulin per 1 mL.
c. U-200 means there are 100 units of insulin per 2 mL.
d. U-100 means there are 100 units of insulin per 100 mL.

70. What is a paradoxical effect in terms of how medication affects certain patients?

a. when a medication has the opposite effect on a person than intended
b. when a medication is not as potent as intended
c. when a medication is stronger for a certain patient than for others
d. when a medication does not work for certain patients

Glossary

A

Absence seizure. Absence of convulsions characterized by a sudden 10- to 30-second loss of consciousness with no falling; formerly called petit mal.

Absorption. Passage of a substance through a body surface into body fluids or tissues.

Acetylcholine. Chemical mediator of nerve impulses in the nervous system.

Achlorhydria. Lack of stomach acid.

Actions. A description of the cellular changes that occur as a result of a drug.

Addiction. Physical and/or psychological dependence on a substance, especially alcohol or drugs, with the use of increasing amounts (tolerance) and withdrawal reactions.

Adjunct. Addition to the course of treatment to increase the efficacy.

Adjuvant. A drug added to a prescription to hasten or enhance the action of a principal ingredient.

Adjuvant Analgesics. A term for a medication (e.g., antidepressants, anticonvulsants) which is not designed to manage pain, but which has effects that can help reduce the need for other analgesics.

Adrenal glands. Glands located adjacent to the kidneys that secrete hormones called corticosteroids.

Adrenergic. Sympathomimetic drug that mimics the action of the sympathetic nervous system.

Adsorbent. Substance that leads readily to absorption.

Adverse drug reactions (ADRs). Unintended side effects from medications such as cough, headache, nausea, and so on.

Adverse effects. Harmful unintended reactions to a drug.

Adverse reactions. A list of possible unpleasant or dangerous secondary effects other than the desired effect.

Albuminuria. Albumin (proteins) in urine.

Allergic reaction. Response of the body resulting from hypersensitivity to a substance (e.g., rash, hives, and anaphylaxis).

Alopecia. Loss or absence of hair.

Alpha-blockers. Drugs that block the alpha$_1$ receptors found in the smooth muscle in the bladder neck and prostate, causing them to relax.

Alzheimer's disease. Dementia characterized by a devastating, progressive decline in cognitive function, followed by increasingly severe impairment in social and occupational functioning.

Aminoglycosides. Drugs used in combination with other antibiotics that treat many infections caused by gram-negative and gram-positive bacteria.

Amnesia. Loss of memory.

Ampule. Glass container with drug for injection; must be broken at the neck to withdraw (via a filter needle if necessary) the drug in solution.

Analeptic. A drug used to stimulate the central nervous system, especially with poisoning by CNS depressants.

Analgesics. Medications that alleviate pain.

Anaphylactic reaction. A life-threatening reaction to a drug, insect/jellyfish sting, snake bite, or foreign substance requiring immediate medical attention.

Anaphylaxis. Allergic hypersensitivity reaction of the body to a foreign substance or drug. Mild symptoms include rash, itching, and hives. Severe symptoms include dyspnea, chest constriction, cardiopulmonary collapse, and death.

Androgens. Male hormones that stimulate the development of male characteristics.

Angina pectoris. Severe chest pain resulting from decreased blood supply to the heart muscle.

Angiogenesis. Development of new blood vessels.

Anorexia. Loss of appetite.

Antacids. Agents that neutralize gastric hydrochloric acid.

Antagonism. Opposing action of two drugs in which one decreases or cancels out the effect of the other.

Antiandrogens. Gonadotropin-releasing hormone analogs that are used to treat prostate cancer.

Antiarrhythmic agents. Drugs that control or prevent cardiac irregularities.

Anticholinergics. Drugs that block the action of the parasympathetic nervous system.

Anticoagulants. Medications used to prevent the formation of clots or decrease the extension of existing clots in such conditions as venous thrombosis, pulmonary embolism, and coronary occlusion.

Anticonvulsants. Medications used to reduce the number or severity of seizures in patients with epilepsy.

Antidepressant. Medications used to treat patients with various types of depression; sometimes called mood elevators.

Antidiabetic. Medications used to lower blood glucose levels in those with impaired metabolism of carbohydrates, fats, and proteins.

Antidiarrheal. Medications that reduce the number of loose stools.

Antidote. Substance that neutralizes poisons or toxic substances.

Antiemetics. Drugs that prevent or treat nausea, vomiting, or motion sickness.

Antiepileptic drug (AED) therapy. Medical therapy aimed at treating and/or reducing seizure activity.

Antiflatulents. Medications used in the symptomatic treatment of gastric bloating or GI gas pain.

Antifungals. Medications used in the treatment of candidal and other specific susceptible fungi.

Antiglaucoma drug. Medications used to lower intraocular pressure.

Antihistamines. Medications that provide symptomatic relief of allergic symptoms caused by histamine release.

Antihypertensives. Medications used in the treatment and management of all degrees of hypertension.

Anti-infective. Medication used in the treatment of infections; includes antibiotics, antifungals, and antivirals.

Anti-inflammatory. Medication used to relieve inflammation.

Antilipemic agents. Drugs that lower the serum cholesterol and low-density lipoproteins (LDLs) and increase the high-density lipoproteins (HDLs).

Antimigraine medication. Medications used to treat or prevent migraine headaches.

Antimuscarinics. Drugs that block cholinergic stimuli at muscarinic receptors. A type of anticholinergic; also called parasympatholytics.

Antineoplastic. An agent that prevents the development, growth, or spread of malignant cells.

Antioxidants. Agents that prevent or inhibit oxidation or cell destruction in damaged or aging tissues. Compounds that fight against the destructive effects of free radical formation.

Antiparkinsonian drugs. Medications used in the treatment of Parkinson's disease to relieve symptoms and maintain mobility but that do not cure the disease.

Antipruritics. Products applied topically to alleviate itching.

Antipsychotic. Major tranquilizers used to relieve the symptoms of psychoses or severe neuroses; sometimes called neuroleptics.

Antipyretic. Medication to reduce fever.

Antiretroviral (ARV) agents. Agents that act against retroviruses such as HIV.

Antiseptics. Substances that inhibit the growth of bacteria.

Antispasmodics. Medications used to reduce the strength and frequency of contractions of the urinary bladder and to decrease gastrointestinal motility.

Antithrombotic agents. Agents that interfere with or prevent thrombosis (clot formation).

Antithyroid. Medication used to relieve the symptoms of hyperthyroidism in preparation for surgical or radioactive iodine therapy.

Antituberculosis agents. Medications used to treat asymptomatic infection and to treat active clinical tuberculosis and prevent relapse.

Antitussives. Medications that suppress coughing.

Antiulcer. Drug that reduces gastric acid secretion or that acts to prevent or treat gastric or duodenal ulcers.

Antivenom injections. Serum that contains antitoxin specific for an animal or insect venom.

Antiviral agent. Medications used to treat viruses, for example, HIV and herpes.

Anxiolytics. Antianxiety medications (tranquilizers) used for the short-term treatment of anxiety disorders, neurosis, some psychosomatic disorders, and insomnia.

Apnea. Cessation of breathing.

Appropriate. Reasonable under the circumstances for a specific patient.

Arrhythmia. An irregular heartbeat that can cause the heart to beat too fast, too slow, or with an irregular rhythm.

Arteriosclerosis. A common arterial disorder characterized by the thickening and loss of elasticity of the arterial walls, resulting in a decreased blood supply, especially to the cerebrum and lower extremities.

Ascites. The abnormal accumulation of fluid in the pleura or peritoneal cavity.

Aspiration. The inhalation of a foreign substance or regurgitated gastric contents into the lungs.

Asthma prophylaxis. Medications used for prophylaxis and the treatment of chronic asthma. Bronchodilators are used for acute asthmatic attacks.

Asymptomatic. Showing no evidence of clinical disease.

Ataxia. Defective muscular coordination, especially with voluntary muscular movements (e.g., walking).

Atherosclerosis. A type of arteriosclerosis characterized by yellowish plaques of cholesterol, lipids, and cellular debris in the walls of large- and medium-sized arteries, resulting in reduced circulation; the major cause of coronary heart disease such as angina pectoris or myocardial infarction.

Atypical antipsychotics. A newer class of antipsychotics with less potential for adverse effects, such as extrapyramidal symptoms and tardive dyskinesia.

Autonomic. Automatic, self-governing, or involuntary nervous system.

B

Bactericidal. Destroying bacteria.

Bacteriostatic. Inhibiting or retarding bacterial growth.

Base. The number that gets multiplied when using an exponent.

Beers list drugs. The most inappropriate drugs for ambulatory nursing home residents and adults 65 years or older.

Benign. Not recurrent or progressive; nonmalignant.

Benign prostatic hyperplasia (BPH). Benign irregular growth of the prostatic glandular tissue that can cause issues with male urination.

Beta-adrenergic blocker. Agent that blocks the beta receptors such as those found in the heart, causing a decrease in the rate and force of cardiac contraction.

Beta blockers. Drugs that block the action of the sympathetic nervous system.

Biotransformation. Chemical changes that a substance undergoes in the body.

Bipolar disorders. Manic-depressive mental disorders in which the mood fluctuates from mania to depression.

Bladder antispasmodics. Agents that treat urinary incontinence by relaxing the bladder and reducing frequent and uncontrolled urination.

Blood dyscrasia. A condition in which any of the blood constituents are abnormal or are present in abnormal quantity.

Bolus. A single, relatively large quantity of medication intended for therapeutic use, such as a bolus dose of a drug injected intravenously.

BPH. Benign prostatic hyperplasia.

BPH therapy. Drugs used to reduce prostate size and associated urinary obstruction and manifestations in patients with BPH.

Bradycardia. Abnormally slow heartbeat.

Bradykinesia. Abnormally slow movement.

Broad spectrum. Antibiotic effective against a large variety of organisms.

Bronchodilators. Medications that relax the smooth muscles of the bronchial tree, thereby relieving bronchospasm and increasing the vital capacity of the lungs.

Buccal administration. In the cheek pouch.

C

C&S. Culture and sensitivity test to identify a causative infectious organism and the specific medicine to which it is sensitive.

Cachexia. Condition of malnutrition and wasting in chronic conditions such as some malignancies and AIDS.

Calculating dosage. Using mathematical computation to determine the correct dosage to administer when a dosage ordered differs from the dose on hand.

Calculus. Stone.

Caplet. An oblong form of a tablet.

Capsule. A special container made of gelatin sized for a single dose of drug.

Carbapenems. A class of broad-spectrum antibiotic drugs, derived from cephalosporins, that resist degradation by bacterial beta-lactamases.

Carbonic anhydrase inhibitors. Drugs that reduce the hydrogen and bicarbonate ions and have a diuretic effect (increasing the excretion of fluids from the body through the urine).

Cardiac glycosides. Medications used primarily in the treatment of heart failure.

Cardiotonic. Increasing the force and efficiency of contractions of the heart muscle.

Cardioversion. Correcting an irregular heartbeat (arrhythmia). Usually accomplished by electrical shock (e.g., defibrillation).

Catecholamines. Mediators released at the sympathetic nerve endings (e.g., epinephrine and norepinephrine).

Cautions. Precautions; steps to take to prevent errors.

Cephalosporins. Semisynthetic antibiotic derivatives produced by a fungus.

Cheilosis. Reddened lips with cracked corners.

Chemical dependency. Condition in which alcohol or drugs have taken control of an individual's life and affect normal functioning.

Chemoinformatics. Application of computer technology, statistics, and math to study information about the structure, properties, and activities of molecules.

Chemotherapy. Chemicals (drugs) with specific and toxic effects upon disease-producing organisms.

Chemotherapy-induced nausea and vomiting (CINV). Vomiting that occurs after the administration of drugs used to treat cancer.

Cholelithiasis. The presence of gallstones in the gallbladder.

Cholinergic. Parasympathomimetic drugs that mimic the action of the parasympathetic nervous system.

Clark's Rule. Weight-based formula to determine proper dosage for children.

Classifications. Broad subcategories for drugs that affect the body in similar ways.

Clone. A copy.

Clonic. Spasm marked by alternate contraction (rigidity) and relaxation of muscles.

Clostridium difficile (C. difficile). Species of bacteria that cause pseudomembranous colitis.

Coanalgesic. Nonopioid analgesic drug that is combined with opioids for more effective analgesic action in relief of acute or chronic pain (e.g., NSAID, acetaminophen).

Coenzyme. Enzyme activator.

Comorbidities. Other serious conditions existing concurrently with the one under discussion.

Comprehensive medication review (CMR). A document provided to a patient by a health care provider that provides an inclusive list of their medications, indications, and directions for use.

Computerized physician order entry (CPOE). Prescriptions are typed into the computer by the prescriber, then printed and signed or sent directly to the pharmacy.

Concomitant. Taking place at the same time.

Concurrent. Existing at the same time.

Confirmation bias. Tendency to favor information that confirms existing beliefs or hypotheses.

Continuous IV infusion. An IV solution that may or may not contain medication that is administered over long periods.

Contraceptives. Medications used for birth control.

Contraindications. Conditions or circumstances that indicate a drug should not be given.

Controlled substances. Drugs controlled by additional prescription requirements because of the danger of addiction or abuse.

Conversion of units. Changing from one system of measurement to another.

COPD. Chronic obstructive pulmonary disease.

Coronary heart disease (CHD). Narrowing of the coronary arteries usually as a result of atherosclerosis.

Coronary vasodilators. Medications used in the treatment of angina. See Vasodilator.

Corticosteroids. Hormones secreted by the adrenal glands that act on the immune system to suppress the body's response to infection or trauma; medications given for their anti-inflammatory and immunosuppressant properties.

COX-2 inhibitor. Anti-inflammatory drug that does not inhibit clotting and causes fewer gastric problems and less GI bleeding than other NSAIDs.

Cryptorchidism. Undescended testicles.

Crystalluria. Crystals in the urine.

Culture and sensitivity (C&S) tests. Performed by medical institutions to reveal what antibiotic class or specific antibiotic will be effective in treating a certain infective organism.

Cumulative effect. Increased effect of a drug that accumulates in the body.

Cushing's syndrome. Excessive production or administration of adrenal cortical hormones, resulting in edema, puffy face, fatigue, weakness, and osteoporosis.

Cutaneous. Pertaining to skin.

Cycloplegic. Drug that paralyzes the muscles of accommodation for eye examinations.

Cytotoxic. Substance that destroys cells.

D

Decongestants. Drugs that constrict blood vessels in the respiratory tract, resulting in the shrinkage of swollen mucous membranes and opened nasal airway passages.

Deficiency. Lacking an adequate amount.

Demulcent. Medication used topically to protect or soothe minor dermatological conditions such as diaper rash, abrasions, and minor burns.

Denominator. The bottom number or divisor of a fraction.

Dependence. Acquired need for a drug after repeated use; may be psychological with craving and emotional changes or physical with body changes and withdrawal symptoms.

Dietary Reference Intakes (DRIs). A system of nutrition recommendations from the Institutes of Medicine of the U.S. National Academy of Sciences.

Digitalization. The process of establishing a loading dose of digitalis for maintaining optimal functioning of the heart without toxic effects.

Diplopia. Double vision.

Direct toxicity. Drug that results in tissue damage; may or may not be permanent.

Distribution. Circulation of drugs, after absorption, to the organs of the body.

Diuresis. The secretion and passage of large amounts of urine.

Diuretics. Medications that increase urine excretion.

Documentation of drug administration. Recording the medication given to a patient on the patient's medical record, including the dose, time, route, and location of injections.

Dosage. Amount of a drug given for a particular therapeutic or desired effect.

Dose-limiting side effects. Those side effects that are serious enough to prevent increasing the dose or level of treatment.

Drug. Chemical substance taken into the body that affects body function.

Drug abuse. The use of a drug for other than therapeutic purposes.

Drug Enforcement Administration (DEA). A bureau of the Department of Justice that enforces the Controlled Substances Act.

Drug form. The type of preparation in which a drug is supplied.

Drug-induced parkinsonism (DIP). The inducement of Parkinson-like symptoms because of drug administration.

Drug interactions. Response that may occur when more than one drug is taken. The combination may alter the expected response of each individual drug.

Drug processes. Four biological changes that drugs undergo within the body.

Drug standards. Federally approved requirements for the specified strength, quality, and purity of drugs.

Dry-powder inhalers (DPIs). Self-generating devices that form a fine aerosol from a powdered drug solution that can then be inhaled using a fast, deep breath into the respiratory system.

Dyskinesia. An impairment of the ability to execute voluntary movements; frequently an adverse effect of prolonged use of some medications, for example, phenothiazines.

Dyslipidemia. Abnormal levels of various blood lipid fractions.

Dysmenorrhea. Painful menstruation.

Dyspepsia. Indigestion.

Dysphagia. Difficulty in swallowing.

Dysphonia. Difficulty speaking or hoarseness.

Dystonic reaction. Spasm and contortion, especially of the head, neck, and tongue, as an adverse effect of antipsychotic medication.

E

e-prescribing (eRX). The manner in which medications are ordered through the electronic medical record.

Effects of drugs. Physiological changes that occur in response to drugs.

Electrolytes. Minerals dissolved in the body fluids.

Electronic medication administration record (eMAR). Medication administration record in the electronic medical record.

Elixir. A usually sweetened, aromatic liquid used in the compounding of oral medicines.

Emetic. Agent that induces vomiting.

Emollient. Medication used topically to protect or soothe minor dermatological conditions, such as diaper rash, abrasions, and minor burns.

Empiric. Best-guess therapy based on history and available clinical information.

Emulsion. A mixture of two liquids that are not mutually soluble.

Endocrine. Internal secretion (hormone) produced by a ductless gland that secretes directly into the bloodstream.

Endogenous. Produced or originating within a cell or organism.

Endorphins. Endogenous analgesics produced within the body.

Enema. The introduction of a solution into the rectum and colon to stimulate bowel activity and cause emptying of the lower intestine.

Enteric-coated tablet. Tablet with a special coating that resists disintegration by the gastric juices and dissolves in the intestines.

Enuresis. Urinary incontinence; bed-wetting.

Enzymatics. Agents that promote the removal of necrotic or fibrous tissue.

Epidural anesthesia. Local anesthetic solution injected into the epidural space just outside the spinal cord.

Epilepsy. A recurrent paroxysmal disorder of brain function characterized by sudden attacks of altered consciousness, motor activity, or sensory impairment.

Epistaxis. Nosebleed.

Erectile dysfunction (ED). The inability to achieve or sustain a penile erection for sexual intercourse.

Estrogen/progestin therapy (EPT). The use of combined hormones for birth control and menopausal symptoms.

Estrogens. Female sex hormones responsible for the development of female secondary sexual characteristics; medications used for many conditions.

Estrogen therapy (ET). The use of the hormone estrogen for the prevention of diseases in woman and relief of menopausal symptoms.

Eunuchism. Lack of male hormone, resulting in high-pitched voice and absence of beard and body hair.

Euphoria. Exaggerated feeling of well-being and elation.

Euthyroid. Normal thyroid function.

Excretion. Elimination of by-products of drug metabolism from the body, essentially through the kidneys, some from the intestines and lungs.

Exogenous. Originating outside the body or an organ, or produced from external causes.

Expectorants. Drugs that increase secretions, reduce viscosity, and help to expel sputum.

Exponent. Number that tells you the number of times a number is to be multiplied by itself.

Extrapyramidal. Disorder of the brain characterized by tremors, Parkinson-like symptoms, dystonic twisting of body parts, or tardive dyskinesia; sometimes associated with prolonged use of antipsychotic drugs and some other CNS drugs.

F

Factor-label method. Method used to convert units of measure.

Fat-soluble vitamins. Vitamins A, D, E, and K.

Febrile seizures. Seizures associated with high temperatures.

Flatulence. Excessive gas in the digestive tract.

Follicle-stimulating hormone (FSH). Hormone that stimulates development of ovarian follicles in the female and sperm production in the testes of the male.

Food and Drug Administration (FDA). An agency within the Department of Health and Human Services that enforces the provisions of the Federal Food, Drug, and Cosmetic Act and amendments of 1951 and 1962.

Free radicals. Unbound compounds that attack and damage the cells or initiate the growth of abnormal cells, resulting in conditions such as cancer or atherosclerosis.

G

Gastric tube administration. Medication administered through a tube in the abdomen to the stomach.

Gastroesophageal reflux disease (GERD). A backward flow of gastric secretions into the esophagus causing inflammation and discomfort. GERD is treated with drugs to accelerate gastric emptying.

Gastroparesis. Partial paralysis of the stomach.

Generic names. General, common, or nonproprietary names of drugs.

GERD. Gastroesophageal reflux disease.

GI antispasmodics. Medications used to help calm the bowel.

Gingivitis. Inflammation of the gums characterized by redness, swelling, and tendency to bleed.

Glaucoma. Abnormal condition of the eye with increased intraocular pressure (IOP) because of obstruction of the outflow of aqueous humor.

Glossitis. Inflammation of the tongue.

Glycosuria. Sugar in the urine.

Goiter. Enlargement of the thyroid gland.

Gout. A form of arthritis in which uric acid crystals are deposited in and around joints.

Grand mal seizures. A form of epilepsy characterized by loss of consciousness, falling, and generalized tonic, followed by clonic, contractions of the muscles. Current term is *tonic-clonic seizure*.

Gray List. List of inappropriate drugs for nursing home residents based on a national survey of geriatric experts.

G-tube or peg tube. Gastric tube, also known as a percutaneous endoscopic gastrostomy (PEG) tube, inserted into the abdomen to administer medications.

Gynecomastia. Enlargement of breast tissue in males.

H

HAART. Highly active antiretroviral therapy for HIV infections.

HAIs. Hospital-acquired infections.

Heart failure. The inability of the heart to circulate blood effectively enough to meet the body's metabolic needs.

Hematological. Concerned with the blood and its components.

Hematopoiesis. Production of blood cells, normally in the bone marrow.

Hematuria. Blood in the urine.

Hepatotoxicity. Damage to the liver as an adverse reaction to certain drugs.

Herbal. Plants or other substances occurring naturally that are available over the counter and are not FDA regulated.

Herbs. Any product intended for ingestion as a supplement to the diet.

Heterocyclic. Second-generation cyclic antidepressants with very different adverse effect profiles.

Hirsutism. Excessive growth of hair in unusual places, especially in females.

Histamine$_2$ blockers. Agents that block the histamine receptors found in the stomach to reduce gastric acid secretions.

Holter monitoring. Patient wears a monitor, which records cardiac rhythms for 24 h.

Homeostasis. Body balance; state of internal equilibrium.

Hormones. Substances originating from an organ, gland, or body part, conveyed through the blood to another body part, and chemically stimulating that part to increase or decrease its functional activity or to increase or decrease the secretion of another hormone.

Hormone replacement therapy (HRT). Estrogen with or without progestin used for osteoporosis prevention and treatment.

Hormone therapy (HT). The therapeutic use of hormones.

Household system. The least accurate way of measuring medications; examples include teaspoons, ounces, and pints.

Household system of measures. Any of the volumes represented by commonly used items as they are applied to administering medicines.

Hyperalimentation. The intravenous infusion of a hypertonic solution containing all of the necessary elements to sustain life. Usually infused through a subclavian catheter into the superior vena cava.

Hypercalcemia. Abnormally high blood calcium.

Hyperglycemia. Abnormally high blood glucose.

Hyperkalemia. Abnormally high potassium in the blood; can lead to cardiac arrhythmias.

Hyperlipidemia. High lipid levels in the blood.

Hyperosmotic. Laxative to draw water from the tissues and stimulate evacuation.

Hyperplasia. An increase in the number of normal cells.

Hyperpyrexia. Extreme elevation of body temperature.

Hypersensitivity. Allergic or excessive response of the immune system to a drug or chemical.

Hyperthyroidism. A condition that occurs when the thyroid gland produces too much thyroid hormone(s).

Hypertension. High blood pressure. One of the major risk factors for coronary artery disease, heart failure, stroke, peripheral vascular disease, kidney failure, and retinopathy.

Hypertonic. A solution that has a greater salt concentration than the body's 0.9 percent.

Hypertriglyceridemia. High triglyceride level in the blood.

Hyperuricemia. Abnormal amount of uric acid in the blood.

Hypnotics. Drugs that promote sleep.

Hypocalcemia. Abnormally low blood calcium.

Hypoglycemia. Abnormally low blood glucose.

Hypokalemia. Abnormally low blood potassium; can lead to cardiac arrhythmias.

Hyponatremia. Decreased sodium in the blood.

Hypotension. Low blood pressure.

Hypotensive. Antihypertensive; medication used in the treatment of hypertension.

Hypothyroidism. Diminished or absent thyroid function.

Hypotonic. A solution that has a lesser salt concentration than the body's 0.9 percent.

Hypoxia. Deficiency of oxygen.

I

Idiopathic. Condition without a known cause.

Idiosyncratic reaction. Unusual reaction to a drug, other than that expected.

Immunomodulators. Drugs that can either stimulate or suppress the immune system to help the body fight infection, cancer, or other diseases.

Immunosuppressant. An agent that decreases or inactivates the immune response to antigens.

Immunosuppressive. Decreases the production of antibodies and phagocytes and depresses the inflammatory reaction.

Indications. List of conditions for which a drug is meant to be used.

Infiltration anesthesia. Local anesthetic solution injected into the skin, subcutaneous tissue, or mucous membranes of the area to be anesthetized.

Inflammatory bowel disease (IBD). The term for a number of chronic, relapsing inflammatory diseases of the gastrointestinal tract of unknown etiology.

Ingestion. To take into the body by mouth through swallowing.

Inhalation drug forms. Forms of a drug to be inhaled by the respiratory system, usually through a specialized device such as a metered-dose inhaler (MDI).

Inhalation route. A route of drug administration through the respiratory system where the large surface area and high vascularity cause a rapid response.

Inhalation therapy. Medications administered through a metered-dose inhaler, small-volume nebulizer, dry-powder inhaler, or intermittent positive pressure breathing apparatus.

Injectable drug forms. Forms of drugs manufactured to be given via injections such as intravenous (IV) or intramuscular (IM).

Injections. The most common form of parenteral administration.

Interactions. Actions that occur when two or more drugs are combined or when drugs are combined with certain foods. See Drug interactions.

Intermittent IV infusion. A small amount (50–100 mL) of IV fluid or medication administered over a short period in prescribed intervals. Sometimes referred to as IV piggyback.

Intra-articular (intracapsular). Injected into the joint.

Intradermal (ID). Injected into the layers of the skin.

Intramuscular (IM). Injected into the muscle.

Intraocular pressure. Pressure within the eyeball.

Intrathecal. Injected into the spinal canal.

Intravenous (IV). Injected into the vein.

Ischemia. Holding back of the blood; local deficiency of blood supply because of the obstruction of circulation to a part (e.g., the heart or extremities).

K

Keratolytics. Agents that promote loosening or scaling of the outer layer of the skin.

Keep Vein Open (KVO). A slow rate of IV fluid administration to maintain the patency of the IV.

Korsakoff's psychosis. Disorder characterized by polyneuritis, disorientation, mental deterioration, and ataxia with painful foot drop, usually associated with chronic alcoholism.

L

Lability. State of being unstable or changeable.

Lacrimation. Discharge of tears.

Laxatives. Drugs that promote evacuation of the intestine.

Legend drug. Available only by prescription.

Leukopenia. Abnormal decrease in white blood cells, usually below 5,000/mm^3 of blood.

Local anesthetic. Medication administered to produce temporary loss of sensation or feeling in a specific area.

Local effect. Affecting one specific area or part.

Lozenge (troche). Tablet that dissolves slowly in the mouth for local effect.

Luteinizing hormone (LH). Hormone that works in conjunction with FSH to induce the secretion of estrogen, ovulation, and development of corpus luteum.

Luteotropic hormone (LTH). Hormone that stimulates the secretion of progesterone by the corpus luteum and secretion of milk by the mammary gland.

M

Macrolides. A class of drugs used in many infections of the respiratory tract, for skin conditions such as acne, or for some sexually transmitted infections when the patient is allergic to penicillin.

Maintenance medications. Medications meant to preserve a desired condition. Drugs used to prevent recurrence or progression of an illness.

Major depressive disorder (MDD). Clinical depression characterized by episodes of all-encompassing low moods, low self-esteem, and loss of interest or pleasure in normally enjoyable activities.

Malignant. Growing worse, resisting treatment; said of cancerous growths.

Medical abbreviations. Symbols used for medication orders.

Medical marijuana. The legal prescribed use of cannabis or its synthetic derivatives (cannabinoids) to treat a disease with symptoms of chronic pain, nausea, and severe decreased appetite.

Medication Errors Reporting (MER) program. The *United States Pharmacopeia* established Medication Errors Reporting (MER) program.

Medication reconciliation. A method used to compare the medications the patient is taking at home to those ordered by the physician when there is a change in care.

Medication-related problems (MRPs). Serious complications resulting from adverse drug reactions.

Medication orders. The physician's prescriptions for the administration of drugs.

Medication therapy management (MTM). The process of a pharmacist or other health care provider reviewing a patient's medications, identifying potential or actual adverse effects or other medication-related problems, and developing a plan to optimize therapy.

MedWatch. A voluntary and confidential program of the Food and Drug Administration for monitoring the safety of drugs, biochemical and medical devices, and nutritional products.

Megadose. Abnormally large dose.

Melena. Blood in the stool.

Meniscus. The bottom of the curve at the top of an amount of liquid when viewed from the side.

Mental impairment. Decreased mental function in older adults frequently caused or worsened by drugs.

Metabolism. Physical and chemical alterations that a substance undergoes in the body.

Metered-dose inhalers (MDIs). Canisters containing a propellant used to deliver a fine mist (aerosol) of a drug into the respiratory system. Often used with a spacer device or reservoir to increase the effectiveness of drug delivery.

Metric system. International standard for weights and measures.

Minerals. Chemical elements occurring in nature and in body fluids.

Miotics. Drugs that cause the pupil to contract.

Mixed number. A number consisting of an integer and a proper fraction.

Mixed seizure. Having more than one type of seizure.

Monoamine oxidase inhibitors (MAOIs). Antidepressant agents used to increase serotonin, norepinephrine, and dopamine levels.

Monoclonal antibodies. Chemotherapy designed to target only cancer cells, thereby sparing normal tissues.

Mortar and pestle. Glass cup with glass rod used to crush tablets.

Motor impairment. A loss or limitation of function in muscle control or movement.

Mucolytics. Medications that liquefy pulmonary secretions.

Myalgia. Tenderness or pain in the muscles.

Mydriatics. Drugs that dilate the pupil.

Myelosuppression. Inhibiting bone marrow function.

Myopathy. Abnormal condition of skeletal muscle.

N

Nasogastric tube administration. Medication administered through a tube inserted through the nose and extending into the stomach.

National Drug Code (NDC) Directory. Provides the FDA with a list of all drugs manufactured for commercial distribution.

Nebulizer (vaporizer). Apparatus for producing a fine spray or mist for inhalation.

Neoplasms. New growth or tumors.

Nephropathy. Disease of the kidneys.

Nephrotoxicity. Damage to the kidneys as an adverse reaction to certain drugs.

Neuroleptic malignant syndrome. Characterized by delirium, rigid muscles, fever, and autonomic nervous system instability.

Neuromuscular blocking agents (NMBAs). Muscle relaxants that cause a direct effect on the muscles, including the diaphragm.

Neuropathy. Any disease of the nerves.

Neurotoxicity. Having the capability of harming nerve tissue.

Neurotransmitters. Substances that travel across the synapse to transmit messages between nerve cells.

Neutropenia. Abnormally small number of neutrophil leukocytes in the blood.

Nonadherence. When a patient does not take one or more medications as prescribed on a regular basis.

Nosocomial. Hospital-acquired infection.

NSAID. Nonsteroidal anti-inflammatory drug.

Numerator. The top number of a fraction.

Nystagmus. Involuntary rhythmic movements of the eyeball.

O

Objective. Referring to symptoms observed or perceived by others.

Official name. Name of the drug as it appears in the official reference, the *USP/NF*; generally the same as the generic drug.

Off-label drug. Drug used in a way not indicated on the FDA label.

Oligospermia. Deficient sperm production.

Onychomycosis. Toenail fungus.

Oophorectomy. Excision of an ovary.

Opioids. Analgesics; controlled substances whose action is similar to opium in altering the perception of pain; can be natural or synthetic.

Opioid antagonists. Drugs used in the treatment of opioid overdoses and in the operating room, delivery room, and newborn nursery for opiate-induced respiratory depression.

Opioid-induced constipation. Constipation that results from opioid drug use slowing transit time in the intestines.

Opportunistic infections. Infections that occur because the immune system is compromised.

Oral drug forms. Drugs manufactured to be given via the oral route such as pills, solutions, and capsules.

Oral medications. Medications administered by mouth.

Oral medication administration. Administering medications by mouth.

Orexin antagonist. Medication that functions by blocking orexin A and B from binding to orexin receptors in the brain. Orexin A and B are chemicals that cause people to stay awake. Blocking these receptors allows for reduced wakefulness, increased duration of sleep, or increased ability to fall asleep.

Orphan drugs. Drugs or biological products used for the diagnosis, treatment, or prevention of a rare disease or condition, that is, one affecting fewer than 200,000 persons in the United States, or greater than 200,000 persons where the cost of developing the drug is probably not recoverable in the United States.

Osmotic agents. Medications used to reduce intracranial or intraocular pressure.

Osteomalacia. Softening of the bones because of inadequate calcium and/or vitamin D.

Osteoporosis. Softening of the bone seen most often in older adults, especially postmenopausal females.

Osteoporosis therapy. Medications used to prevent or treat osteoporosis by increasing bone mineral density.

Otic. Referring to the ear.

Otitis media. The most common type of otic infection; located in the middle region of the ear.

Ototoxicity. Damage to the eighth cranial nerve, resulting in impaired hearing or ringing in the ears (tinnitus); adverse reaction to certain drugs.

Overactive bladder (OAB). A sudden intense urge to urinate that may or may not lead to loss of the urine.

Overdose. A higher-than-normal amount sufficient to cause toxicity.

Over-the-counter (OTC) medication. Medication available without a prescription.

Oxytocin. Hormone that stimulates the uterus to contract, thus inducing childbirth.

P

Palliative. Referring to the alleviation of symptoms, but not production of a cure.

Paradoxical. When a medication has the opposite effect on a person (or group of persons) compared to average adults.

Paradoxical reaction. Opposite effect from that expected.

Paraphilia. A psychosexual disorder in which unusual or bizarre imagery or acts are necessary for the realization of sexual excitement.

Parasympatholytics. Anticholinergics; medications that decrease the chemical that promotes bronchospasm.

Parenteral. Any route of administration not involving the gastrointestinal tract (e.g., injection, topical, and inhalation).

Paresthesia. Numbness, tingling, or a "pins and needles" feeling, especially in the extremities.

Parkinsonism. A neurological disorder with symptoms resembling Parkinson's disease (e.g., muscle rigidity, tremor).

Parkinson's disease. A chronic neurological disorder characterized by fine, slowly spreading muscle tremors, rigidity and weakness of muscles, and shuffling gait.

Partial seizures. Also known as focal seizures. The onset is limited to one area of the brain.

Pedophilia. Sexual attraction to children.

Pellagra. A disease caused by the deficiency of niacin (nicotinic acid), characterized by skin, gastrointestinal, mucosal, neurological, and mental symptoms.

Penicillins. A class of antibiotics produced from certain species of a fungus.

Percutaneous endoscopic gastrostomy (PEG) tube. Feeding tube inserted in the stomach.

Percutaneous endoscopic gastrostomy (PEG) tube medication. Feeding tubes, or PEG tubes, that allow you to receive medication or nutrition through your stomach.

Peripheral. Away from the center. Usually refers to the extremities.

Peripheral nerve block. Local anesthetic solution injected into or around nerves or ganglia supplying the area to be anesthetized.

Pharmacogenomics. The study of the effects of genetic differences among people and the impact that these differences have on the uptake, effectiveness, toxicity, and metabolism of drugs.

Pharmacology. The study of drugs and their origin, nature, properties, and effects on living organisms.

Photosensitivity. Increased reaction, for example, burn, from brief exposure to the sun or an ultraviolet lamp.

Physiological dependence. Physical adaptation of the body to a drug and withdrawal symptoms after abrupt drug discontinuation.

Phytoestrogen. A plant substance with estrogen-like properties.

Piggyback. Also known as secondary infusion is the administration of medication that is diluted in a small volume of IV solution through an established primary infusion line.

Placebo. Inactive substance given to simulate the effect of another drug; physical or emotional changes that occur reflect the expectations of the patient.

Placebo effect. Relief from pain as the result of suggestion without active medication.

Platelet inhibitors. Class of drugs that inhibit platelet aggregation (clumping) to prevent clots.

Poison. A toxic substance that is taken into the body by ingestion, inhalation, injection, or absorption and that can cause illness, injury, or death.

Polypharmacy. Excessive use of drugs or prescription of many drugs given at one time.

Postherpetic neuralgia. Nerve pain following an episode of shingles.

Postoperative nausea and vomiting (PONV). One of the most commonly occurring postoperative complications. During the postoperative period, patients may experience considerable pain, difficulty moving, nausea, and vomiting.

Potentially inappropriate medications (PIMs). Medications listed under "Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults."

Potentiation. Increased effect; action of two drugs given simultaneously is greater than the effect of the drugs given separately.

Precautions. List of conditions or types of patients that warrant closer observation for specific side effects when given a drug.

Prevention of medication errors. Rules to follow to avoid making mistakes.

Priapism. Prolonged penile erection.

Primary generalized seizure. A classification of seizures in which widespread electrical discharges occur in the brain, involving both sides of the brain.

Probiotics. Agents having favorable or health-promoting effect on living cells and tissues; for example, *Lactobacillus acidophilus*, present in the GI tract, is probiotic because its presence inhibits the growth of harmful bacteria.

Prodrugs. Inert drugs that exhibit their pharmacological activity only after biotransformation.

Progesterone. Hormone responsible for changes in uterine endometrium in the second half of the menstrual cycle in preparation for implantation of the fertilized ovum, development of maternal placenta after implantation, and development of mammary glands; medication with several uses.

Progestins. Synthetic drugs that exert progesterone-like activity.

Proliferation. Rapid reproduction.

Proportion. Two ratios that are equal.

Protectants. Medication used topically to protect or soothe minor dermatological conditions, such as diaper rash, abrasions, and minor burns.

Proton pump inhibitor (PPI). Gastric antisecretory agent unrelated to H_2 receptor antagonists used for short-term symptomatic relief of GERD, ulcers, heartburn, and erosive esophagitis.

Prototype. A model or type from which subsequent types arise (e.g., an example of a drug that typifies the characteristics of that classification).

Pruritis. Itching.

Psychomotor epilepsy. Also known as temporal lobe epilepsy or focal seizures because of the area in the brain that is involved. Characterized by temporary impairment of consciousness; confusion; loss of judgment; and abnormal acts, even crimes and hallucinations—but no convulsions.

Psychotropic. Any substance that acts on the mind.

Pyrosis. Heartburn.

Q

Quinolones. A class of antibiotics used in adults for the treatment of some infections of the urinary tract, lower respiratory tract, gastrointestinal tract, skin, bones, and joints.

R

Racemic. Mixture that is composed of equal amounts of dextrorotatory and levorotatory forms of the same compound. One form is active and one inactive.

Ratio. A relationship between two numbers.

Reconstitution. The return of a substance previously altered for preservation and storage to its original state, as is done with dried blood plasma and powdered medications.

Rectal drug forms. Drugs manufactured to be administered via the rectal route, such as suppositories.

Rectal medications. Medications in suppository or liquid form administered as a retention enema.

Rectal Route. Enteral route of medication administration that allows for rapid and effective absorption of medications via the highly vascularized rectal mucosa.

Refractory. A disorder resistant to treatment.

REM. Rapid eye movement or dream phase of sleep.

Reporting of medication errors. Notifying the FDA of serious adverse events or product quality problems associated with medications (MedWatch).

Rescue treatment. Treatment used in an emergency situation, such as a severe asthma attack, to give quick relief of symptoms.

Resistance. An organism's lack of response to antibiotics when they are used too often or treatment is incomplete.

Responsibilities. Needed for safe and accurate administration of medication; include knowledge, judgment, and skill.

Responsibilities of drug administration. Duty to administer drugs safely and accurately.

Restless legs syndrome (RLS). A condition marked by an intolerable creeping sensation or itching in the lower extremities, causing an almost irresistible urge to move the legs.

Retention enema. An enema that may be used to provide nourishment, medication, or anesthetic.

Reye's syndrome. Complication following acute viral infections in those under 18 years of age; characterized by rash, vomiting, and confusion about a week after the onset of a viral illness. May lead to respiratory arrest. Aspirin may induce Reye's syndrome when administered to children or adolescents with viral infections.

Rhabdomyolysis. An acute, sometimes fatal, disease characterized by the destruction of muscle; leads to renal failure.

Route of delivery. The way that drugs are taken into the body.

S

Scurvy. A vitamin C deficiency disease usually resulting from a lack of fresh fruits and vegetables in the diet. Symptoms include ulcerated gums and mouth, loose teeth, muscle cramps and weakness, poor healing, and bruising.

Sedatives. Controlled substances used to promote sedation in smaller doses; some may be used to promote sleep in larger doses.

Selective distribution. Affinity or attraction of a drug to a specific organ or cells.

Selective norepinephrine reuptake inhibitors (SNRIs). Antidepressants that block the reabsorption of the neurotransmitter norepinephrine, thus helping to restore the brain's chemical balance.

Selective serotonin reuptake inhibitors (SSRIs). Antidepressants that block the reabsorption of the neurotransmitter serotonin, thus helping to restore the brain's chemical balance.

Sentinel event. Patient safety event that results in death, permanent harm, or severe temporary harm.

Serotonin syndrome. A potentially life-threatening reaction to excessive serotonin activity in the central nervous system.

Shared Clinical Decision Making (SCDM). A collaborative process where a patient and their healthcare provider work together to make treatment decisions.

Side effects. Unpleasant or dangerous secondary effects of medications.

Seven "Rights" of medication administration. Guidelines for giving medication that include the right medication, right amount, right time, right route, right patient, right technique, and right documentation.

Skeletal muscle relaxants. Medications used to treat some musculoskeletal disorders associated with pain, spasm, abnormal contraction, or impaired mobility.

Small-volume nebulizers (SVNs). Devices that create a fine mist of a drug solution using a gas source (aerosolization). The aerosol is then inhaled via a mouthpiece or mask.

Smoking-cessation aids. Medications used to slowly lower the level of nicotine while the patient participates in a behavior modification program for smoking cessation.

Solution. A liquid containing a dissolved substance.

Somogyi effect. Hyperglycemic rebound, usually a result of frequent overdoses of insulin, which causes an accelerated release of glucagon.

Sources of drugs. Five ways that drugs are obtained.

Spinal anesthesia. Local anesthetic solutions injected intrathecally (into the subarachnoid space of the spinal canal) either in the lumbar region or in the lower region (saddle block), depending on the area to be anesthetized.

Status asthmaticus. Persistent and intractable asthma.

Status epilepticus. Continual attacks of convulsive seizures without intervals of consciousness.

Stevens–Johnson syndrome. A severe, sometimes fatal, inflammatory disease affecting children and young adults; characterized by ulcers on the skin and mucous membranes, fever, and painful joints.

STI. Sexually transmitted infection.

Stomatitis. Inflammation of the mucous membranes of the mouth.

Subcutaneous (subcu, SC, or SQ). Beneath the skin.

Subjective. Perceived by the individual, not observable by others.

Sublingual (SL) administration. Administering a medication by placing it under the tongue.

Sulfonamides. A class of anti-infectives used in combination with other drugs to slow the development of resistance; used in the treatment of urinary tract infections, enteritis, and opportunistic infections of AIDS.

Sulfonylureas. A class of oral medications used to treat type 2 diabetes by stimulating the pancreas to release insulin.

Sulfonylureas. Oral antidiabetic drugs for the treatment of type 2 diabetes.

Superinfection. A new infection with different resistant bacteria or fungi. Usually associated with certain types of antibiotic therapy.

Supplements. Products intended for ingestion as an addition to the diet.

Suppository. A semisolid substance for introduction into the rectum, vagina, or urethra, where it dissolves.

Suspension. A state of a solid when its particles are mixed with, but not dissolved in, a fluid or in another solid; also, a substance in this state.

Sustained-release capsule or tablet. Capsule or tablet containing drug particles that have various coatings (often of different colors) that differ in the amount of time required before the coatings dissolve.

Sympathomimetic. Adrenergic drug that mimics the action of the sympathetic nervous system.

Symptoms of overdose. Symptoms caused by a higher-than-normal amount of drugs sufficient to cause toxicity.

Syncope. A brief lapse in consciousness; fainting.

Synergism. Action of two drugs working together for increased effect.

Synthetic. Prepared in the laboratory by artificial means.

Syrup. A concentrated solution of sugar in water to which specific medicinal substances are usually added.

Systemic effect. Affecting the whole body or system.

T

Tablet. Disk of compressed drug.

Tachycardia. Abnormally fast heartbeat.

Tachypnea. Abnormal rapidity of respiration.

Tall Man Lettering. A method of writing drug names to help differentiate between look-alike and sound-alike drugs. Example: CeleXA and CeleBREX.

Tardive dyskinesia (TD). Slow, rhythmical, stereotyped involuntary movements such as tics.

Telephone order (TO). An order for treatment medication via the phone. Some agencies allow only certain health care practitioners to take telephone orders. All phone orders should be read back for accuracy, and a physician must sign the order within 24 h.

Temporal lobe seizures. See Psychomotor epilepsy.

Teratogenic effect. Effect of a drug administered to the mother that results in abnormalities in the fetus.

Testosterone. Male hormone; medication used for replacement therapy and other purposes.

Tetracyclines. Broad-spectrum antibiotics used in the treatment of infections caused by rickettsia, chlamydia, or some uncommon bacteria.

Therapeutic range. A range of drug levels in the blood that will produce the desired effects without causing serious side effects.

Thrombocytopenia. Abnormal decrease in the number of blood platelets.

Thrombolytic agents. Medications used to dissolve clots after they have formed.

Timed-release capsules (sustained-release [SR] or extended-release [ER]). Capsules containing many small pellets that are dissolved over a prolonged period of time.

Tinnitus. Ringing in the ears.

Tocolysis. Suppression of uterine contractions in preterm labor.

Tolerance. Decreased response to a drug after repeated dosage; greater amounts of the drug are required for the same effect.

Tonic. Muscular tension resulting in *extension* of the trunk and extremities, sometimes followed by synchronous *contractions* of the muscles (clonic spasm).

Tonic-clonic seizure. Seizure characterized by an abrupt loss of consciousness and falling, with tonic extension of trunk and extremities.

Topical. Applied to a specific area for a local effect to that area only (e.g., applied to the skin or mucous membranes).

Topical drug forms. Drugs used for dermal and mucosal application.

Topical anesthesia. Application of a local anesthetic directly to the surface of the area to be anesthetized.

Toxicity. Condition resulting from exposure to a poison or a dangerous amount of a drug.

Toxicology. Study and detection of toxic substances, establishing treatment and methods of prevention of poisoning.

Trade names. Names by which a pharmaceutical company identifies its products; brand names.

Tramadol. A synthetic opioid used for the treatment of moderate to severe pain, it is a partial antagonist at the mu receptor which decreases its risk for abuse compared to other opioids.

Transcutaneous. Across the skin, as in transdermal medication delivery to the body by slow absorption through the skin.

Transdermal. Patch containing the medicine is applied to the skin; the drug is absorbed through the skin over a prolonged period of time.

Tricyclics. Antidepressants that elevate the mood, have a mild sedative effect, and increase appetite.

U

Unilateral seizures. Seizures that affect only one side of the body.

Unit-dose form. Each dose of the medicine is prepackaged in a separate packet, vial, or prefilled syringe.

Uricosuric agents. Promote urinary excretion of uric acid.

Urinary analgesic. Medication used to relieve burning, pain, and discomfort in the urinary tract mucosa.

Urinary anti-infectives. Drugs used for initial or recurrent urinary tract infections caused by susceptible organisms, usually bacteriostatic instead of bactericidal.

Urticaria. Hives.

U.S. Recommended Dietary Allowances (U.S. RDAs). Vitamins and minerals necessary for the maintenance of good nutrition in the average healthy adult under normal living conditions in the United States.

V

Vaccines. Suspensions containing antigenic molecules derived from a microorganism, given to stimulate an immune response to an infectious disease.

Variables. Factors that affect the speed and efficiency of drugs processed by the body.

Vasoconstrictors. Drugs that narrow blood vessels, resulting in increased blood pressure; used in the treatment of shock.

Vasodilator. A drug that expands the walls of the blood vessels, improving blood flow and resulting in the lowering of blood pressure.

Verify your calculations. Confirm the result of calculations with another professional, such as an instructor.

Vertigo. Dizziness; lightheadedness.

Vial. Glass container with rubber stopper that must be punctured with a needle to withdraw a drug solution or to reconstitute a drug in powdered form.

W

Water-soluble vitamins. B-complex vitamins and vitamin C.

Wernicke's syndrome. Mental disorder characterized by the loss of memory, disorientation, and confusion; usually associated with old age or chronic alcoholism.

Withdrawal. Cessation of administration of a drug, especially an opioid or alcohol, to which a person has become physiologically and/or psychologically addicted; withdrawal symptoms vary with the drug used.

X

Xanthine. Medication that indirectly increases the chemical that causes bronchodilation; also a respiratory stimulant to increase the ventilatory drive.

Xerophthalmia. Dryness of the eyes.

Xerostomia. Dryness of the mouth.

Y

Young's Rule. An age-based formula for calculating pediatric dosages.

Z

Z-track method. A specific type of injection procedure used for medications (such as iron injections) that are irritating to the tissues.

Index

Всё для победы!
НАРОДНЫЙ ФРОНТ
https://pobeda.onf.ru/
LET'S HELP THE RUSSIA

Note: Italicized page numbers indicate illustrations.

A

Abacavir, *37*, *565*
Abbreviations, 63–69
    apothecary system, 69
    for medication orders, *64–65*
Abnormal Involuntary Movement Scale (AIMS), 423, *424*, *425*
Abreva, 213
Absence seizures, 460, 462–464
Absorption, 29, 31, 593–594, 604
Acarbose, *499*
Acetaminophen, 18, 21, 386, *388*
Acetazolamide, *369*
Acetylcholine, 227
Acetylcysteine, *341*
Acetylsalicylic acid. *See* Aspirin
Aclidinium, *335*
Acne agents, 221
Acne medications, 219, *220*
Acne papules, *220*
Acne scarring, *220*
Actions, as drug heading, 22
Activase, *274*
Activated charcoal, 159
Actonel, 450
Acute (angle-closure) glaucoma, 363
Acute coronary syndrome (ACS), 271
Acute respiratory disorders, 480
Acyclovir, 213, 217, 562–563, *564*
Adalat CC, *255*
Adalimumab, *314*
Addiction, 429
Adenocard, 244, *250*
Adenosine, 244, *250*
Adenosine diphosphate (ADP) receptor antagonists, 271–272
Adherence, 601
Adjuvant analgesics, 378, 380, 389, *391–392*
ADME (absorption, distribution, metabolism, excretion), 29
Administration
    medication errors, 99–100
    principles of, 100–104
    rights of, 100
    safety responsibilities for, 98
Administration routes, 36–39, 103
ADP receptor antagonists, *274*
Adrenal corticosteroids, 480–482, *482*
Adrenalin, *230*
Adrenergic blockers, 231, *232*, 233
Adrenergic medications, *230*
Adrenergic receptors, 228
Adrenergics, 228–230, 243, 246
Adrenocorticotropic hormone (ACTH), 479
Advanced Cardiac Life Support (ACLS), 51
Adverse drug effects, 39
Adverse Drug Reactions (ADRs), 39

Adverse reactions, 536
  as drug heading, 22
  reporting, 104
Age, drug processing and, 33
Agency for Healthcare Research and Quality (AHRQ), 100
Age-related medication issues
  drugs to avoid with certain medical conditions, 596–598
  issues with adherence, 601
  older adult considerations, 593
  pediatric considerations, 602–604
  physiologic changes with increasing age, 593–595
  polypharmacy, 599–601
  potentially inappropriate medication use in older adults, 596
Aggrenox, 271, *274*
AHFS Drug Information, 89, 98
AIDS (acquired immunodeficiency syndrome), 565–569, *565–566*
Albuterol sulfate, *334*
Alcohol, 429–432
Alcohol abuse, *430*
Alcohol poisoning, 431–432
Aldactone, 282
Alendronate, 450, *452*
Alfuzosin, *296*
Alkylating agents, 577
Allantoin, 288
Allergic contact dermatitis, *205*
Allergic hypersensitivity, 536
Allergic reactions
  as adverse drug effect, 19, *41*
  to insect bites, 160
  oral administration and checking for, *112*
Allopurinol, 288, *289*
Almotriptan, *394*
Alogliptan, *500*
Alpha-adrenergic blockers, 231, *232*, *256*
Alpha-agonists, 364, 367, *369*
Alpha-blockers, 231, 295
Alpha-glucosidase inhibitors, 496, *499*
Alpha-linolenic acid (ALA), 264
Alprazolam, *421*
Altace, *255*
Alteplase, 272, *274*
Alternative medicines
  dietary supplements, 193, 194–195, 199
  fraudulent products, 195
  herbs and other dietary supplements, 193, 197–199
  quality products, 195–196
  reading and reporting, 195–196
Aluminum hydroxide gel, *306*
Alzheimer's disease
  agents for, 472–474, *474*
  monoclonal antibodies, 474
Amantadine, 469, *471*
American Academy of Clinical Toxicology, 159
American Academy of Pediatrics (AAP), 158, 174
American Association of Poison Control Centers, 158
American College of Chest Physicians, 174
American Medical Association, 163
American Pharmaceutical Association (AphA), 24
Amikacin, *546*
Aminoglycosides, 540–541, *546*
Amiodarone, 244–245, 247–248, *250*
Amiodipine, *256*
Amitriptyline, *391*, *414*
Amlodipine, *255*
Ammonium lactate, *209*
Amoxicillin, *547*
Amoxicillin-clavulanate, *547*
Amphetamine, 32, 404–406, *408*, 434–435
Ampicillin, 85, *547*
Ampicillin-sulbactam, *547*
Ampule, 57, *58*
Anabolic steroids, 8
Analgesics, 378–383, *383–384*, *388–389*, *391–392*
  adjuvant, 378, 380, 389, *391–392*
  nonopioid, 385, *388–389*
  opioid, 379–383, *383–384*
  tramadol, 382–383, *384*
Anaphylactic reactions, 40
Anaphylactic shock, 230
Anaphylaxis, 536
Androgen agents, *509–510*
Androgens, 508–509

Anemia, 188, 273
Angina, 53, 125, 126, *127*, 257–258, 268, 271
Angiotensin-converting enzyme (ACE) inhibitors (ACEIs), 251–252, *256*
Angiotensin receptor blockers (ARBs), 255, *256*
Animals, as source of drugs, *28*
Antabuse, 431
Antacids, 34, 243, 248, 252, 301, *306*
  vitamin C and, 178–180
Antagonism, 34
Antara, *265*
Antiadrenergic agents, 253, *255*
Antiandrogens, 294, 581
Antiarrhythmic agents
  adenosine, 244, *250*
  amiodarone, 244–245, 247–248, *250*
  beta-adrenergic blockers, 245–246, 251, *254*
  calcium channel blockers, 246–247, 251
  lidocaine, 247, 250
  overview, 243–244
  procainamide, 247–248, 250
  propafenone, 249, 250
Antibacterial agents, 214, *214*, *217*
Antibiotic duration of therapy, 540
Antibiotics, 538, 540
  as drug classification, 16
Anticholinergic agents, 468–469
Anticholinergics, 235, 291, *293*, 307, *314*, 321, 333, *335*, 468, *471*
Anticoagulants, 16, 266, 267–268, 269–270
Anticonvulsants, 390–391, 458–460, *463–464*
  first-generation, 460–462
  second-generation, 463
Antidepressants, 409–414, *414–416*
  as drug classification, 16
Antidiabetic agents
  alpha-glucosidase inhibitors, 496, *499*
  biguanides, 494–495, *499*
  GLP-1 agonists, 496–497
  hyperglycemia, 492–493
  hypoglycemia, 493–494
  insulin, 489–494, *491*
  meglitinides, 497, *500*
  oral and injectable noninsulin, 494, *499–500*
  overview, 488–489
  SGLT2 inhibitor therapy, 498–499, *500*
  sulfonylureas, 495–496, *499*
  thiazolidinediones, 498, *500*
Antidiabetics, 16
Antidiarrheal agents, 310–313, *314*
Antidopaminergics, 321–322
Antidotes, 159
Antiemetics, 47, 321–323, *323*
Antiepileptic drug (AED) therapy, 462
Antiestrogens, 581
Antiflatulents, 313, *314*
Antifungals, 212–213, *213*, 541–542, *546*, 550–551, *555*
Antiglaucoma agents, 363–369, *363*, *369–370*
Antiglaucoma drugs, 364
Antigout medications, *289*, *296*
Antihistamines, 205, 344, *345*, 362, 395–396
  for anaphylactic reaction, 40
  first generation, 345–346, *348*
  second generation, 346–347, 349
Antihypertensives, 16
  angiotensin-converting enzyme (ACE) inhibitors (ACEIs), 251–252, *256*
  angiotensin receptor blockers (ARBs), 252–253, *255*, *256*
  antiadrenergic agents, 253, *255*
  beta-adrenergic blockers, 251, *254*
  calcium channel blockers, 251, *255*
  overview, 251
  peripheral vasodilator, 253–254, *255*
  thiazide diuretics, 251
Anti-infective drugs
  adverse reactions, 536
  agents for VRE, 557–558, *558*
  aminoglycosides, 540–541, *546*
  antibiotics, 538, 540
  antifungals, 550–551, *555*
  antituberculosis agents, 552–554, *555*
  antivirals, 562–564, *564–565*
  carbapenems, 545, *547*
  cephalosporins, 541–542, *546*
  clindamycin, 556
  eye medications, 358–360
  HIV/AIDS, 565–569, *565–566*
  immunizations, 537–538
  macrolides, 542–543

Anti-infective drugs (*continued*)
  metronidazole, 556
  overview, 534
  penicillins, 544–545, *547*
  quinolones, 547–548, *554–555*
  resistance, 535–536
  selection of, 535–536
  sulfonamides, 560, *562*
  tetracyclines, 549, *555*
  urinary, 561, *562*
  vaccines, 537
  vancomycin, 557
Anti-inflammatory agents, 204, 444–447, *447–448*
  eye medications, 360–362, *362*
  skeletal, 441–444
Antilipemic agents, *265*
  bile acid sequestrants, 262–263, *265*
  cholesterol absorption inhibitor, 264, *265*
  fibric acid derivatives, 263–264, *265*
  nicotinic acid, 263, *265*
  omega-3 fatty acids, 264–265
  overview, 260–261
  statins, 261–262, *265*
Antimanic agents, 416–417, *417–418*
Antimetabolites, 576
Antimigraine agents, 378, 392–393, *394–395*
Antineoplastic drugs
  alkylating agents, 577
  antiandrogen, 581
  antibiotic, 580
  antiestrogen, 581
  antimetabolites, 576
  antitumor antibiotics, 580
  biological therapies, 581–582
  cautions and responsibilities, 585–586
  colony-stimulating factors, 582
  corticosteroids, 580–581
  cytotoxic danger to health care personnel, 588
  hormones and hormone modifiers, 580–581
  interferons, 582
  mitotic inhibitors, 577–578
  monoclonal antibodies, 582–583
  overview, 573
  paclitaxel, 578
  radioactive isotopes, 585
  side effects, *587*
  targeted therapies, 583
  taxanes, 578
  vaccines, 584–585
Antioxidants, 192
Antiparkinsonian drugs, 465–470, *470–471*
Antipruritics, 204–205, *205*, *208–209*
Antipsychotic medications, 422–427, *426–427*
Antipyretics, 47, 385
Antiretroviral (ARV) agents, 566
Antiretroviral protease inhibitors, 566–567
Antiseptics, 215, *216*
Antispasmodics, 290, 307, *314*
Antithrombotic agents, 266–272
  adenosine diphosphate (ADP) receptor antagonists, 271–272
  anticoagulants, 266, 267–268, 269–270
  aspirin, 271–272
  dipyridamole, 271
  heparin, 268–269, 270
  platelet inhibitor therapy, 270–271
  warfarin, 266–267
Antithyroid agents, 486, *488*
Antituberculosis agents, 552–554, *555*
Antitumor antibiotics, 580
Antitussives, 342–343, *344*
Antiulcer, 301
Antivenom injections, 161
Antivirals, 213, *214*, *217*, 562–564, *564–565*
Anxiolytics, 418–421, *421–422*
Apixaban, 268
Apothecary system, 69
Appli-Ruler paper, 126
Aquasol A, 170
Aqueous solutions, 47
Aranesp, 273, *274*
Arformoterol, *334*
Aripiprazole, *427*
Arixtra, *270*
Armodafinil, 406
Arrhythmias, 243
Ascorbic acid, 178–179, 182
Ascriptin, *274*
Asenapine, *427*
Ashwagandha, *197*

Aspirin, 20, 83, 271, *274*
  classification of, 16
  drug facts label, *7*
Asthma prophylaxis, 338–339, *340*
Astragalus, *197*
Ataxia, 419
Atazanavir, *565*
Atenolol, 251, 254
Athlete's foot, *212*
Ativan, 460
Atogepant (Qulipta), 394
Atomoxetine, *409*
Atorvastatin, 261, *265*
Atorvastatin/amlodipine, *265*
Atropine, *236*, *371*
  sulfate, 84
Attention-deficit hyperactivity disorder (ADHD), 253, 404, 405, 407
Atypical antipsychotics, 422
Auranofin, *28*
Autonomic nervous system (ANS) drugs
  adrenergic blockers, 231, *232*
  adrenergics, 228–230
  cholinergic blockers, 235–237, *236*
  cholinergics, 233–234
  overview, 225, 226
Avanafil, *512*
Azathioprine, 37
Azelastine, *348*
Azilect, 468
Azithromycin, *546*
Azulfidine, 309

B

Bacitracin, *217*
Baclofen, *443*
Bactericidal, 215
Bactrim, *28*
Barbiturates, 247, 267, 396
Barrel, of syringe, 131, *132*
Barrett, Stephen, 195
Baths, 146
Beclomethasone, *337*
Beers list drugs, 596
Benadryl, 22, 40, 88, *209*, 345, 395
Benazepril, *255*
Benicar, *255*
Benign (noncancerous), 574
Benign prostatic hyperplasia (BPH), 23, 294, *294*
Benzocaine, *208*
Benzodiazepines (BZDs), 396–397, *398–399*, 418–420, *421–422*
Benzonatate, *344*
Benzoyl peroxide, *220*
Benztropine, *471*
Beriberi, 174–175
Beta$_2$ receptors, 245
Beta-adrenergic blockers, *232*, 245–246, 251, *254*, *256*, 364, 366–367, *369*
Beta-blockers, 16, 231, 251, *254*
Beta carotene, 170–171, *180*
Betadine, 215
Betaxolol, *369*
Bethanechol, *234*, 291, *293*
BiDil, 253, *260*
Biguanides, 494–495, *499*
Bile acid sequestrants, 262–263, *265*
Bimatoprost, *370*
Biological therapies, 581–582
Bipolar disorder, 416, *416*
Birth control. *See* Contraceptive agents
Bisacodyl, 110, *320*
Bismuth subsalicylate, 310–311, *314*
Bisphosphonates, 450, *452*
Bitter orange, 195
Bladder antispasmodics, 289–290
Blood-brain barrier, 31
Blood clots, 261
Body composition, 604
Bolus, 49, 51
BPH. *See* Benign prostatic hyperplasia (BPH)
Bradycardia, 243, 251
Brilinta, *274*
Brimonidine, *369–370*
Brinzolamide, *369*
Broad spectrum, 545
Bromocriptine, *470*
Bronchodilator administration, 330–331
Bronchodilators, 330–334, *334–335*
Buccal administration, 37, 125

Buccal tablet, 54
Budesonide, *337*
Bulk-forming laxatives, 315, *320*
Bumetanide, 281, *284*
Bumex, 281
Bupropion, 352, *353*, *415*
Burn medications, 146, 217–219, *218*, *220*
Buspirone, *422*
Butorphanol, *383*
Butyrophenone, *426*
Bystolic, *254*

C

Caduet, *265*
Caffeine, 404
Caffeine citrate, *408*
Calan, 250, *256*, 259
Calan SR, *255*
Calciferol, 171–172
Calcitonin, 451
Calcitonin gene-related peptide (CGRP) pathway, 394
Calcitriol, 172
Calcium, 186–187, 190
Calcium carbonate, 186, *306*
Calcium channel blockers, 246–247, 251, *256*
Calculation
  for dosage, 82–85
  guidelines, 82–83
  verify accuracy, 83
Calculator, 78
Calculus, 280
Calming antidepressant, 414
Canagliflozin, *500*
Canakinumab, 289, *289*
Cancer cells, *573*
Cancer treatments. *See* Antineoplastic drugs
Cannabidiol (CBD), 193
  forms, 194
  potential adverse effects, 194
  potential beneficial effects, 193
Capsules, 45, 46, *48*
Carafate, 305
Carbamazepine, 37, *391*, *417*, *463*
Carbapenems, 545, *547*
Carbidopa/levodopa, 466–467, *470–471*
Carbonic anhydrase inhibitors (CAIs), 364–365
Carbon monoxide poisoning, 159–160
Carboprost, *529*
Cardiac arrhythmias, 240, 244
  calcium and, 186
  hyperkalemia and, 185
Cardiac glycosides, 241–243, *250*
Cardiovascular disease (CVD), 250, 598
Cardiovascular system medications
  antiarrhythmic agents, 243–250
  anticoagulants, 266–270
  antihypertensives, 250–253
  antilipemic agents, 260–265
  antithrombotic agents, 266–272
  cardiac glycosides, 241–243, *250*
  colony stimulating factors, 273
  coronary vasodilators, 257–260
  platelet inhibitors, 270–271, 274
  thrombolytic agents, 272, 274
Cardizem, 46, 246
Cardizem CD, *255*
Cardizem LA, *255*
Cariprazine, *427*
Carisoprodol, *443*
Carpuject, 135, *135*
Carvedilol, *256*
Cascara sagrada, *197*
Catapres, 253, *255*
Catapres TTS, *255*
Catechol-*O*-methyl-transferase (COMT) inhibitors, 470, *471*
Cathartics, 315
Cathflo Activase, *274*
Cat's claw, *197*
Cautions, 22
CCR5 antagonists, *566*, 568–569
Cefaclor, *546*
Cefazolin, *546*
Cefdinir, *546*
Cefepime, *546*
Cefotaxime, *546*
Cefoxitin, 287
Ceftaroline, *546*
Ceftazidime, *546*
Ceftazidime/avibactam, *546*
Ceftolozane/tazobactam, *546*

Ceftriaxone, *546*
Celebrex, 20, 445
Celecoxib, 445, *448*
Celexa, 20
Center for Drug Evaluation and Research (CDER), 24
Centers for Disease Control and Prevention (CDC) National Immunization Program, 24
Central nervous system (CNS) stimulants, 404–407, *408–409*
Cephalexin, *546*
Cephalosporins, 46, 541–542, *546*
Cerebrospinal fluid, amphetamines and, 32
Cetirizine, *349*
Cevimeline, *234*
Chamomile, *197*
Chantix, 352
Chapparal, 195
Charcoal, for poisoning victims, 159
Chelation, 31
Chemical dependency, 429
Chemical name, 17
Chemoinformatics, 27
Chemotherapy, 574
Chemotherapy-induced nausea and vomiting (CINV), 322
Children
  dosages, 89–90
  drug processing and, 33
  poison and, 158, 162
  poisoning and, 158
Chlordiazepoxide, *421*
Chlordiazepoxide hydrochloride, 18
Chlorhexidine, *217*
Chloride, 184, 190
Chloride channel activators, 318, *320*
Chlorofluorocarbon (CFC), 330
Chlorpheniramine, *348*
Chlorpromazine, *426*
Chlorpropamide, *499*
Cholecalciferol, 171–172, 181
Cholesterol, 261
Cholesterol absorption inhibitor, *265*
Cholestyramine, 245, 262, *265*
Cholinergic blockers, 235–237, *236*
Cholinergic drugs, 233, 234
Cholinergic medications, *234*
Cholinergics, 291–292
  as autonomic nervous system drugs, 233–234
Cholinesterase inhibitors, 473, *474*
Chronic (open-angle) glaucoma, 364
Cimetidine, 176, 246, *306*
Cinnamon, *197*
Cipro, 372–373, 547–548
Ciprofloxacin, 547–548, *554*
Citalopram, *415*
Clarithromycin, *547*
Clark's Rule, 89
Classifications. *See* Drug classifications
Clemastine, *348*
Clindamycin, 556, *559*
Clonazepam, 20, *421*
Clonidine, 20, 253, *255*
Clopidogrel, *274*
Clorazepate, *421*
Clostridium difficile infection, 313, *313*
Clotrimazole, *216*
Clozapine, *427*
CNS stimulants, 404–407
Coal tar, *209*
Coanalgesic, 385
Cobalamin, 176–177
Cocaine, 436
Codeine, 19, *28*, *383*
Cognitive impairment, 597
Colchicine, 286, *289*
Colesevelam, 262, *265*
Collagenase, 207, 208, *209*
Colony-stimulating factors (CSFs), 273, 582
Combination drugs, 19
Comfrey, 195
Common wart, *207*
Comprehensive medication review (CMR), 600
Computerized physician order entry (CPOE), 68
COMT (catechol-O-methyl-transferase) inhibitors, 470, *471*
Confirmation bias, 104
Conjugated estrogens, *517*
Conjugated estrogens/medroxyprogesterone, *517*
Consumer Reports, 195
Consumer safety, drugs and, 2–11

Continuous IV infusion, 145
Contraceptive agents, 517–519, *523*
  choice of, 520–522
  postcoital, 522
  progestin-containing intrauterine device, 521
  progestin-only, 521
Contraindications, as drug heading, 22
Controlled substances, 8, 21
  documentation for, 103
  prescriptions for, 2
  recordkeeping, 11
  schedules, 6, *8*, *9*
Controlled Substances Act (1970), 8
Conversion of units, 72
Cordarone, 244, *250*
Coreg, 251, *254*, *256*
Coreg CR, 254
Coronary heart disease (CHD), 260–261
Coronary vasodilators, 257–260
Corticosteroids, 205–206, *206*, *209*, 286, 480
  for anaphylactic reactions, 40
  as anti-inflammatory, 360–361, *360*
  antineoplastic, 580–581
  inhaled, 336, *337*
  interaction of loop diuretics, 282
  intranasal, 336–337, *337*
  ophthalmic, 146–147
  for respiratory system, 336–337, *337–338*
Cortisone, *482*
Cortisporin, 372
Cosyntropin, *482*
Cough-cold-allergy products safety, 349–350
Coumadin, 266
Coumarin derivative, *269*
COX-2 inhibitors, 445–447, *448*
Cozaar, *255*, *256*
Cranberry, *197*
Creams, *52*, 146
  vaginal, 53
Crestor, *265*
Cromolyn sodium, *340*
CSFs, *274*
C&S tests. *See* Culture and sensitivity (C&S) tests
Cubicin, 558
Culture and sensitivity (C&S) tests, 534
Cumulative effect, 32, 593
Cyanocobalamin, 176–177, 182
Cyclobenzaprine, *443*
Cyclopentolate, *371*
Cycloplegic, 370
Cyclosporine, *362*
CYP3A4 inhibitor, 394
Cytotec, 305
Cytotoxic, 574

D

Dabigatran, 267, *270*
Dalteparin, 268, *270*
Danazol, *509*
Dantrolene, *443*
Dapagliflozin, *500*
Dapsone, *220*
Daptomycin, 558, *559*
Darbepoetin alfa, *274*
Darifenacin, *293*
Darunavir, *565*
DAW (dispense as written), 18
DEA registration number, 8
Decimal place value chart, *80*
Decimal points, 82, 85, 91
Decimals, 80–81
Decongestants, 347–348, *349*, 362
Deep vein thrombosis (DVT), 268, 519
Deficiency, vitamin, 171
Delivery routes, 44
Deltoid site, 140, *142*
Demadex, 281
Demerol, *28*, 83–84, 86, 90
Denominator, 79, 80
Denosumab, 451, *453*
Depakene, 462
Depakote, 462
Dependence, 40, 380
Depressants, 3
Dermal patches, *127*
Dermal route, 39
Desipramine, *391*, *414*
Desloratadine, *349*
Desvenlafaxine, *415*
Detrol, 290

Dexamethasone, *362*, *482*
Dexlansoprazole, *307*
Dextroamphetamine, *408*
Dextromethorphan (DXM), 19, 436
Diabetes mellitus (DM), 488, 489
Diabetic foot ulcers, 208
Diazepam, 113, *421*
Dibucaine, *208*
Dibucaine ointment, 29
Diclofenac, *447*
Dicloxacillin, *547*
Dicyclomine, 307, *314*
Dicylomine, *236*
Dietary Approaches to Stop Hypertension (DASH), 251
Dietary Reference Intakes (DRIs), 169–170
Dietary Supplement Health and Education Act of 1994 (DSHEA), 3, 193
Dietary supplements, 193, 194–195
  safety of, 3
Digitalis, *28*
Digoxin, 32, 231, 241–243, 245, *250*
Dilantin, 113
Dilatrate (SR), *260*
Diltiazem, 246, 251, *255*, 259, 262
Diltiazem SR, *255*
Dimenhydrinate, *323*
Dinoprostone, *529*
Diovan, *255*, *256*
Diphenhydramine, 22, *209*, *344*
Diphenhydramine hydrochloride, 22
Diphenoxylate with atropine and loperamide, 311
Diphenydramine, *349*
Diprolene, *209*
Dipyridamole, 271, *274*
Dipyridamole with aspirin, *274*
Direct toxicity, 536
Disopyramide, 247
Dispense as written (DAW), 18
Distribution, 29, 31–32, 593, 594, 604
  selective, 32
Disulfiram, 431
Disulfuram-like reactions, 556
Ditropan, 290
Diuretics, *284*
  as drug classification, 16
  loop, 281–282
  osmotic agents, 283
  overview, 279
  potassium-sparing, 282–283
  thiazides and other, 281
DNA, as source of drugs, *28*
Docosanol, 213, *217*
Documentation
  for administration, 103
  medication orders, *64–65*, 65
Docusate, *320*
Dolasetron, *323*
Donepezil, *474*
Dopamine, *230*
Dopamine agonists, 467, *470–471*
Dopamine replacement, 466–467
Dorzolamide, *369*
Dosage, 35
  administration and, 101–102
  calculation guidelines, 82–83
  defined, 35
  drug distribution and, 29
  error prevention, 91
  geriatric, 91
  preparation of, 74
  schedule of, 102
  usual, 22
Dose-limiting side effects, 577
Douche solution, 54
Doxazosin, *232*, 295, *296*
Doxepin, *414*
Doxycycline, *555*
Doxycycline hyclate, 18
DPP-4 inhibitors, 497
Dronabinol, *389*
Drug actions, terms indicating, 21–23
Drug addiction, 429
Drug administration, abbreviations for, 45
Drug classifications
  for Alzheimer's disease, 472–474, *474*
  decongestants, 347–348
  eye medications, 358–372
nutritional concepts of pharmacology, 167
–199 osteoporosis therapy, 449–452, *452–*
453 overview, 16

Drug classifications (*continued*)
  restless legs syndrome agents, 472
  sedatives and hypnotics, *398–399*
  vitamins, minerals, and herbs, 167–199
Drug Enforcement Administration (DEA), 8, 10, *68*
Drug errors, 19, 20
Drug forms
  defined, 44
  inhalable, 56
  injectable, 47–52, *49*
  mucosal, 53
  oral, 45–47, *48*
  rectal, 47
  and right medication, 100–102
  safety devices, 60
  standard, 45–56
  supplies, 56–60, *57–58*
  topical, 52–54, *52*, 53
Drug history, 3–4
Drug-induced parkinsonism (DIP), 466
Drug inserts, 6, 9
Drug interactions, 22, 34–35
Drug label, 21
Drug laws, 5–9
  Controlled Substances Act, 8
  FDA and DEA, 10
  Federal Food, Drug, and Cosmetic Act and Amendments of 1951 and 1962, 6
  health care practitioners and, 10–11
  Omnibus Budget Reconciliation Act, 9
  Orphan Drug Act, 9
  Pure Food and Drug Act, 5
Drug packages, 9
Drug preparation. *See* Drug forms
Drug processes, 29
Drugs
  administration routes, 36–39
  allergic reactions to, 19, *41*
  dosage, 35
  effects of, 29
  errors, 19
  interactions, 34–35
  Internet as reference, 23–24
  legal terms referring to drugs, 20–21
  legend, 6
  orphan, 9
  physiologic changes with age, 593–595
  processing by the body, 29–33
  reference sources for, 9, 23
  sources of, 27, *28*
  terms indicating actions, 21–23
  unexpected responses to, 39–41
Drug standards, 5
Drug therapy
  for absence seizures, 462–464
  for febrile seizures, 462
  for generalized and partial seizures, 460–462
Dry-powder inhalers (DPIs), 56, 128, 331, *331*
Duexis, 302
Dulaglutide, *499*
Duloxetine, *391*, *415*
Duodenal ulcer, 304
Duragesic, 53, 126
Dutasteride, *296*
Dyazide, 19
Dyrenium, 282
Dysphagia, 110

E

Ear drops, 53, 373
Ear medications, 148–149, *148*
  ear wax building and blockage, 374, *374*
  otitis media, 372
  systematic preparations for ear infections, 374
  topical preparations for ear infections, 372–373
Echinacea, *197*
Ecotrin, *274*
Efavirenz, *566*
Effient, *274*
Eicosapentaenoic acid (EPA), 264
Eldepryl, 468
Electrolytes, 183
Electronic drug references, 23
Electronic medication administration record (eMAR), 23, 68, *69*
Eletriptan, *394*
Eliquis, 267
Elixir, fluid extract, 47
Emesis, 159, 321

Emetic, 158
Emollients, 206, *209*, 316
Empagliflozin, *500*
Empiric, 534
Empty stomach, drug absorption and, 31
Emulsion, 46
Enalapril, *255*, *256*
Endocrine system drugs
  adrenal corticosteroids, 480–482, *482*
  antidiabetic agents, 488–499, *499–500*
  overview, 478
  pituitary hormones, 479–480, *479*
  thyroid disorders, 483–487, *488*
Endorphins, 379
Enema solution, 47
Enfuvirtide, *566*
Enoxaparin, 103–104, *270*
Entacapone, *471*
Enteral, 37
Enteral route, 37
Enteric-coated tablets, 45–46
Enzyme preparations, 207–208, *209*
Eosinophilic asthma agents (IL-5 monoclonal antibodies), 339
Ephedra, 195
Ephedrine, 243
Ephedrine alkaloids, 195
Epidural injection, 51
Epilepsy, 458
Epinephrine, 40, 160, *230*, *335*
Epi-pens, 41
Epitonin, 195
Epocrates, 23
Epoetin alfa, *274*
Epogen, 273, *274*
e-prescribing (eRx), 68
Erectile dysfunction agents, *511–512*
Erectile dysfunction medications, 510–511, *511–512*
Ergocalciferol, 171–172
Ertugliflozin, *500*
Erythromycin, *547*
Erythropoiesis-stimulating agents (ESAs), 273, *274*
Escitalopram, *415*
Esomeprazole, *307*
Esterified estrogens, *517*
Estradiol, *517*
Estradiol/norethindrone, *517*
Estrogen- and progestin-containing vaginal rings, 521–522
Estrogen and progestin therapy (EPT), 512
Estrogen–progestin contraceptives, 520–521, *520*
Estrogens, 267, 451, 512–515, *517*
Estrogen therapy (ET), 512
Eszopiclone, *398*
Ethambutol, *555*
Ethosuximide, *463*
Etodolac, *448*
Evista, 451
Excretion, 29, 32–33, 593, 595, 604
Exenatide, *499*
Expectorants, 340–341, *341–342*
Extrapyramidal side effects (EPS), 422
Extravasation, 579
Eye drops, 53
Eye medications, 146–147, *147*
  administration, *360*
  antiglaucoma agents, 363–369, *363*, *369–370*
  anti-infective drugs, 358–360
  anti-inflammatory agents, 360–362, *362*
  local anesthetics, 371, *371*
  mydriatics, 370–371, *371*
Eye ointment, 53
Eyes, external poisoning of, 160
Ezetimibe, 264, *265*
Ezetimibe/simvastatin, *265*

F

Factor-label method, 72
Factor Xa inhibitors, 267, *268*
Famciclovir, *564*
Famotidine, *306*
Fat-soluble vitamins, 169, 170–174, 180–182
FDA MedWatch, 196
Febrile seizures, 460, 462
Febuxostat, 288, *289*
Federal Food, Drug, and Cosmetic Act (1938), 5, 6
Fenofibrate, 263, *265*
Fentanyl, 126
Fentanyl citrate, *383*

Fentanyl transdermal, *383*
Fenugreek, *198*
Fesoterodine, *236*, *293*
Fetal alcohol syndrome (FAS), 431
Fetal malformations, vitamin A and, 171
Fexofenadine, *349*
Fibrates, 262, 263–264
Fibric acid derivatives, 263–264, *265*
Fibrillation, 243
Fidaxomicin, *547*
Filgrastim, *274*
Finasteride, *296*
First-generation anticonvulsants, 460–462, *464*
First generation antihistamines, 345–346, *348*
Fish oil, *265*
Flomax, 295
Floxin, 372
Fluconazole, 550–551, *555*
Fludrocortisone, *482*
Fluid extract, 47
Flumazenil, 159
Flunitrazepam, 437
Fluorometholone, *362*
Fluoxetine, *415*
Fluphenazine, *426*
Flurbiprofen, *362*
Focal seizures, 458, 460
Folic acid, 177, 182
Follicle-stimulating hormone (FSH), 507
Fondaparinux, *270*
Food and Drug Administration (FDA), 210, 405, 584
  children, poison, and, 163
  drug pregnancy categories, 39
  establishment of, 6
  on herbal remedies and dietary supplements, 3
  MedWatch and, 104, 196
  online resources, 24
  reporting adverse effects to, 104
Food in stomach, drug absorption and, 31
Food labels, 191, *191*
Formoterol, *334*
Forteo, 451
Fosamax, 450
Fosphenytoin, *463*
Fractions, 79–80
Fragmin, *270*
Free radicals, 192
Frovatriptan, *394*
Furosemide, 281, *284*
Fusion inhibitors (FIs), *566*, 568

G

Gabapentin, *392*, *464*
Galantamine, *474*
Garlic, *198*
Gastric lavage, 159
Gastric mucosal agents, 304–305, *305*
Gastric tube administration, 110
Gastroesophageal reflux disease (GERD), 302, 303, *306*
Gastrointestinal conditions, 598
Gastrointestinal (GI) administration, 38, 45
  gastric tube, 110
  nasogastric tube, 110, 118–120, *118*
  oral, 109–110, 111–114, *111–113*, *115*
  overview, 109–110
  rectal, 110, 116, *117*
Gastrointestinal (GI) drugs
  antacids, 301–302
  anticholinergics, 307–308, *314*
  antidiarrheal agents, 310–313, *314*
  antiemetics, 321–323, *323*
  antiflatulents, 313, *314*
  antispasmodics, 307–308, *314*
  antispasmodics/anticholinergics, 307–308, *314*
  gastric mucosal agents, 304–305, 304–307, *306*
  for inflammatory bowel disease (IBD), 307–310, *309*, *314*
  laxatives, *320–321*
  prophylaxis, 321
  for treatment of ulcers and reflux, 302–304
Gauge, needle, 58–59, 138, 139
GC-C agonists, 310, *314*
G-CSF, *274*
Gelatin capsules, *48*
Gemfibrozil, 34, 263, *265*
Gender, drug processing and, 33
Generalized seizures, primary, 458, 458–460
Generic equivalents, 18
Generic name, 17–19

Gene therapy, 27
Gentamycin, *546*
Geriatric dosage, 91
Ginger, *198*
Ginkgo (GBE), *198*
Ginseng, *198*
Glaucoma, 253, 258. *See also* Antiglaucoma agents
Glimepiride, *499*
Glipizide, *499*
GLP-1 agonists (incretin mimetics), 496–497
Glucocorticoids, 310
Glucosamine, *198*
Glucovance, 19
Glyburide, 19, *499*
Glyburide/metformin, *500*
Glycerine, *320*
Goldenseal, *198*
Gonadotropics, 507–508
Gonadotropin-associated drugs, *530*
Gonadotropin-releasing hormones (GnRHs), 529, *530*
Gout, 285
  medications for, 285–288, *286*
Grams, 70, *71*
Granisetron, *323*
Granulocyte colony-stimulating factor (G-CSF), 273
Graves' disease, *487*
Growth hormone, 27, *28*
G-tube, 110
Guaifenesin, 19, 341, *342*
Guanfacine, *409*

H

Hallucinogens, 436
Haloperidol, 422, *426*
Handbook of Nonprescription Drugs, 23
Handwashing, 100, 111, *111*
Health care practitioners
  law and, 10–11
  as source of drug information, 3
Heart attack, 261
Heart failure, 241
Helicobacter pylori treatment, 305, *305*
Hematopoiesis, 273
Hematopoietic agents, 273
  colony stimulating factors (CSFs), 273
  erythropoiesis-stimulating agents (ESAs), 273
Heparin, 110, 140, 174, 268–269, *270*
Hepatitis B, 60
Hepatitis B vaccine, 27, *28*
Hepatitis C, 60
Herbal supplements, 3, 193
Herbs, 197–199
Heroin, 35, 433–434
Heterocyclic antidepressants, 413, *415*
High-density lipoproteins (HDLs), 261
Histamine$_2$ blockers (H$_2$ blockers), 302, *306*
HIV (human immunodeficiency virus), 262, 272, 565–569, *565–566*
HMG-CoA reductase inhibitors, 261
Homatropine, *236*
Hormone replacement therapy (HRT), 451
Hormones, 451, *452*, 478
Hormones and hormone modifiers, 580–581
Hormone therapies (HTs), 512, 513–514
Household measurement, 74
Household system, 69, 72
Hub, of needle, 132
Human chorionic gonadotropin (hCG) hormone, 32
"Human Drugs,," 24
Human growth hormone (HGH), 479
Hydralazine, 253, *255*, *256*, *260*
Hydrochlorothiazide, *256*, *284*
Hydrocodone, *383*
Hydrocodone-containing products, 382
Hydrocortisone, *482*
Hydromorphone, *383*
Hydroxyzine, *422*
Hyperglycemia, 492–493
Hyperkalemia, 185, 282
Hypersensitivity, 40
Hypertension, 251
Hyperthyroidism, 486
Hypertonic, 284
Hypnotics, *398–399*
Hypodermic syringe, 59
Hypoglycemia, 493–494
Hypokalemia, 280
Hypotension, 251
Hypothyroidism, 483, 484, *484*

Hypotonic, 284–285
Hytrin, 295

I

Ibandronate, *452*
Ibuprofen, 29, *447*
Idiosyncrasy, 39
Illegal drug abuse, 433–437
Illegal drugs, consumer safety issues and, 5
Imdur (SR), *260*
Imipramine, *414*
Immunizations, 537–538
Immunodeficiency virus, needle sticks and, 60
Immunosuppressant, 480
Immunosuppressive properties, 574
Impetigo, *214*
Implantable devices, 54–56
Inderal, 246, *254*
Inderal LA, *254*
Indications, as drug heading, 22
Indirect toxicity, 536
Individual pill crusher and pill cutter, 57, *57*
Indomethacin, *448*
Inflammatory bowel disease (IBD), 307–310, *309*, *314*
Infliximab, *314*
Ingestion, poisoning by, 158
Inhalable drug forms, 56
Inhalation administration, 37, 38
Inhalation, poisoning by, 159–160
Inhalation route, 128–131, *128*
Inhalation therapy, 128
Inhaled corticosteroids, 336, *337*, 340
Injectable drug forms, 47–52, *49*
Injection administration, 131–144
  drawing up medications, 136, *136–137*
  intradermal, 132, 137, *138*
  intramuscular, 132
  needles, 132–133, 135
  routes, 36–37
  subcutaneous, 132, *138*, 139, *139*
  syringes, 132–133, *133*, 134–135, *134*, *135*
Injection port, 47
Injections
  safety devices, 60
  syringes, *58*, 59–60, *59*
Insect bites, 40
Institute for Safe Medication Practices (ISMP), 65, 100
Insulin, *28*, 37, 110, 133, *134*, 489–494, *491*, *501–502*
Insulin pen, 133
Insulin syringe, 133, *134*
Integrase inhibitor, *566*, 569
Integumentary system medications, 203–204
  acne medications, 219, *220*
  antibacterial agents, 214, *214*, *217*
  antifungals, 211–212, *212*
  antipruritics, 204–205, *205*, *208–209*
  antiseptics, 215, *217*
  antivirals, 213, *214*, *217*
  burn medications, 217–219, *218*, *220*
  corticosteroids, 205–206, *206*, *209*
  emollients, 206, *209*
  enzyme preparations, 207–208, *209*
  keratolytics, 207, *208*, *209*
  local anti-infectives, 211–215, *216–217*
  pediculicides, 210, *211*
  protectants, 206, *209*
  scabicides, 209–210, *211*, *216*
Interactions, drug, 22
Interferons, 582
Intermittent IV infusion, 145–146
International Normalized Ratio (INR), 267
Internet, as source of drug information, 23–24
Intracapsular (intra-articular) injection, 52
Intracapsular route, 37
Intracardiac route, 37
Intradermal (ID) injections, 51, 133, 137, *138*
Intradermal (ID) route, 37
Intramuscular (IM) injections, 50, 132, *141*
Intramuscular (IM) route, 37, 39
Intranasal corticosteroids, 336–337, *337*
Intraocular pressure, 364
Intraosseous injection, 51
Intraspinal injection, 51–52
Intraspinal route, 37
Intrauterine devices (IUDs), progestin-containing, 521
Intravenous (IV) bolus/push, 145
Intravenous (IV) infusions/IV drip, 50
Intravenous (IV) injection, 49–50, *49*

Intravenous (IV) piggyback (IVPB), *49*, 50, 145
Intravenous (IV) push, *38*, *49*
Intravenous (IV) route, 37–38
    medication, 145–146
Intraventricular injection, 51
Intraventricular route, 37
Intrinsic factor, vitamin B_{12} absorption and, 176
Iodine, 159, 191
Ipecac syrup, 158
Ipratropium bromide, *335*
Irinotecan, 37
Iron, 187–188, *191*
Iron dextran, 188
Iron supplements, poisoning and, 161
Ischemia, 257
ISMP List of Error-Prone Abbreviations, Symbols, and Dose Designations, 65, *66–67*
Isocarboxazid, *415*
Isoniazid, *555*
Isophane (NPH), 490
Isoproterenol, *230*, 243, 246
Isoptin SR, *255*
Isopto Homatropine, *236*
Isordil, *259*, *260*
Isosorbide, *259*, *260*
Isosorbide dinitrate, *260*
Isosorbide dinitrate with hydralazine, *260*
Isosorbide mononitrate, *260*
Isotretinoin, 170, *220*
Isotretinoin Medication Guide, 219
Isuprel, *230*
Ivermectin, *216*

J

Jantoven, *269*

K

Kava, 195, 198
Keflex, 47
Keratolytics, 207, *208*, *209*
Ketoconazole, *216*
Ketorolac, *362*, *448*
Kidneys, drug excretion and, 32
Kinetics, 29
Krystexxa, 288

L

Labels
    drug, 5, 6
    warning, *30*
Labor and delivery drugs
    magnesium sulfate, 528
    methylergonovine, 527
    mifepristone, 526–527
    oxytocin, 524–525, *529*
    prostaglandins, 525–526, *529*
    terbutaline, 527–528, *529*
Lactobacillus acidophilus, 314
Lactobacillus GG, *314*
Lactulose, *320*
Lamivudine/zidovudine, *565*
Lamotrigine, *392*, *417*, *464*
Lanoxin, *250*
Lansoprazole, *307*
Lasix, 281
Lasmiditan, 394, *395*
Latanoprost, 368, *370*
Laxatives, 315–319, *320–321*
    bulk-forming, 315, *320*
    emollients, 316
    osmotic, 317–318, *320–321*
    saline, 317, *319*
    stimulant, 317, *320*
    stool softeners, 315–316
Legal accessibility, 20
Legal terms referring to drugs, 20–21
Legend drug, 6, 21
Lemborexant, *399*
Lethal dose, 35
Leucovorin, 576
Leukotriene inhibitors, 338–339, *340*
Levalbuterol, *334*
Levaquin, 547–548
Levetiracetam, *464*
Levocetirizine, *349*
Levodopa, 176
Levofloxacin, 547, *554*
Levomilnacipran, *415*
Levophed, *230*
Levothyroxine (T4), *488*
Lexi-Drugs, 23

Librium, 18
Lidocaine, *209*, 247, *250*, *388*
Lidocaine patch, 387, *387*
Lidoderm, *209*
Lifitegrast (Xiidra), 361
Linaclotide, *314*
Linagliptin, *500*
Lindane, *216*
Linezolid, *559*
Liniment, 52
Liothyronine (T3), *488*
Lipid (fat) solubility, drug absorption and, 31
Lipid-lowering agents, 16
Lipitor, 261, *265*
Liquid injectable drug form, 47
Liquid measurement, 72, *72*
Liquid medications, preparation of, 115–116
Liraglutide, *499*
Lisdexamfetamine, *408*
Lisinopril, *255*
Lithium, 252, 416–417, *417*
Loading dose, 35
Local anesthetics, 371, *371*, 386–387, *387*
Local anti-infectives, 211–215, *216–217*
Local effects, 29, 125
Lofibra, *265*
Lomotil, *28*
Look-alikes, poisons and, 162, *162*
Loop diuretics, 281–282, *284*
Loperamide, *314*
Lopid, 34, 263, *265*
Lopinavir/ritonavir, *565*
Lopressor, *250*, *256*
Loratadine, *349*
Lorazepam, *422*
Losartan, *256*
Lotensin, *255*
Lotions, 52, 146
Lovastatin, *265*
Lovastatin/niacin, *265*
Lovaza, *265*
Lovenox, 103, *270*
Low-density lipoproteins (LDLs), 261
Low-molecular-weight heparins (LMWHs), 268–269, *270*
Lozenge (troche), 46, *48*
Lubiprostone, *320*
Luteinizing hormone (LH), 513
Luteotropic hormone (LTH), 508
lymphocyte function-associated antigen-1 (LFA-1) antagonist, 361

M

Macrolides, 243, 542–543
Mafenide, *220*
Magnesium, *190*
Magnesium hydroxide, *320*
Magnesium sulfate, 528
Ma huang, 195
Maintenance dose, 35
Maintenance medications, *331*
Malabsorption syndromes, 169
Malignancies, corticosteroids and, 480
Malignant (cancerous), 574
Marijuana, 435–436
Mast cell stabilizers, 339, *340*
Mavik, *255*
Maximum dose, 35
Measurement, systems of, 69–73
Meclizine, *323*
Medical abbreviations, 63
Medical conversion, 72–73
Medic-Alert tag or bracelet, 40
Medical marijuana, 387–388
Medical personnel, role in combatting drug abuse, 437
Medical Products Reporting Program, *105–106*
Medication Administration Record, 112, *112*
Medication errors
  administration and, 99–100
  prescription legibility and, *68*
  prevention of, 91
  reporting, 100
Medication Errors Reporting (MER) program, 100
Medication, IV, 145–146
  continuous IV infusion, 145
  intermittent IV infusion, 145
Medication orders, *64–65*, 65
Medication reconciliation, 100, 448
Medication-related problems (MRPs), 593
Medications

disposal of, 163
drawing up, 136, *136–137*
patient education concerning, 2–3
Medication therapy management (MTM), 600
Medicine cup, 57
MED-NEBs, 129
Medroxyprogesterone, *517*
MedWatch, 104, *105–106*, 196
Megadoses, of vitamins, 169
Megestrol acetate, *517*
Meglitinides, 497, *500*
Melatonin receptor agonists, 397–398, *399*
Meloxicam, *448*
Memantine, *474*
Mental impairment, 597
Meperidine, 83–84, 86, 87, 90, *383*
Meropenem, *547*
Meropenem/vaboractam, *547*
Mesalamine, 309, *314*
Metabolism, 32, 593, 594–595, 604
Metaxalone, *443*
Metered-dose inhalers (MDIs), 56, 128, *128*, 330, *330*
Metformin, 19, *499*
Methadone, *384*
Methimazole, 486
Methocarbamol, *443*
Methotrexate dosing, 576
Methylergonovine, 527, *529*
Methylphenidate, *408*
Methylphenidate preparations, 404–406
Methylprednisolone, *482*
Methyltestosterone, *509*
Metoclopramide, *323*
Metolazone, *284*
Metoprolol, *250*, *256*, *259*
Metoprolol succinate, *232*
Metoprolol tartrate, *232*
Metric system, 69, 70–72
Metronidazole, *217*, 556, *559*
Mevacor, *265*
Micafungin, 551, *555*
Micardis, *255*
Miconazole, *216*
Microzide, *256*
Midazolam, 420, *422*
Mifepristone, 526–527
Miglitol, *499*
Migraine, non-triptan agents, 394
Milk of Magnesia, *28*
Milk thistle, 198
Milligrams, *71*, 72
Milnacipran, *391*, *415*
Mineral oil, *320*
Minerals
  antioxidant, 192
  calcium, 186–187, 190
  defined, 183
  as drug source, *28*
  indications for supplements, 169
  iodine, 191
  iron, 187–188, *191*
  magnesium, *190*
  potassium, 184–185, 190
  sodium and chloride, 184, *190*
  zinc, 189, 191
Minimum dose, 35
MINI-NEBs, 129
Minipress, *256*
Minitran, *260*
Minocycline, *555*
Miotics, 147, 364, 365–366, *369*
Mirabegron, 290, *293*
Mirtazapine, 414, *416*
Misoprostol, 304–305, *307*, *529*
Mist, 56
Mitotic inhibitors, 577–578
Mixed numbers, 79
Mixed seizure, 460
Modafinil, 406, *408*
Model example, 17
Mometasone, *338*
Monoamine oxidase-B (MAO-B) inhibitors, 467, *471*
Monoamine oxidase inhibitors (MAOIs), 410, 411–412, *415*
Monoclonal antibodies, 289, *289*, 310, *314*, 451, *453*, 582–583
Montelukast, *340*
Morphine, *28*, 87–88
Morphine sulfate, *384*
Motion sickness, dermal patches for, 53, *127*

Movantik, 320
Moxifloxacin, *555*
Mucolytics, 340–341, *341–342*
Mucosal drug forms/administration, 53
Multiple-dose vials, 58
Mupirocin, *217*
Mydriatics, 147, 370–371, *371*
Myocardial infarction, 250, 271
Myocardial infarction with ST-elevation, 271
Myrbetriq, 290

N

Nabilone, *389*
Nabumetone, *448*
n-Acetylcysteine, 159
Naloxegol, 319, *320*
Naloxone, 34, 35, 159
Names, of drugs, 17–19
Naproxen, *448*
Naratriptan, *394*
Narcan, 34, 35
Narcotic analgesics, 16
Narcotic antitussive, 342, *344*
Narcotics, 3
Narrow therapeutic index drugs, 486
Nasacort Allergy 24HR (OTC), 21
Nasal corticosteroids, *345*
Nasogastric tube administration, 110, 118–120, *118*
Nasogastric tube (NGT), 118–120, *118*
Nasonex 24HR allergy, 21
Nateglinide, *500*
National Academy of Sciences, 169
National Council Against Health Fraud, 195
National Drug Code (NDC) Directory, 6
National Formulary (NF), 5
National Immunization Program, 24
National Institutes of Health (NIH), 24, 171, 432
National Library of Medicine, 24
Nebivolol, *254*
Needles, 58–59, *58*
  parts of, 132
  recapping, *137*
Needle-stick injuries, 60
Neomycin, 31, 243
Neostigmine, *234*
Nephrotoxicity, 22
Nervous system, *226*
Netarsudil (Rhopressa), 369
Neupogen, *274*
Neuraminidase inhibitors, 563–564
Neuroleptic malignant syndrome, 466
Neuromuscular blocking agents (NMBAs), 443
Neurotransmitters, 226, 228, 409
New drug application (NDA), 18
Niacin, 263, *265*
Niacinamide, 178
Niaspan, *265*
Nicoderm, 53
Nicotine, *352*
Nicotine replacement therapy, 351–352, *351*
Nicotinic acid, 178, 182, 263, *265*
Nifedipine, *255*
Nitro-Bid, 258, *260*
Nitro-Dur, 126, 258, *260*
Nitrofurantoin, 561, *562*
Nitroglycerin, *52*, 53, 126, *259*, *260*
Nitroglycerin ointment, 126, *127*
Nitrolingual spray, *260*
Nitrostat tabs S.L., *260*
NMDA receptor antagonists, 473–474, *474*
Nonadherence, 601
Nonbenzodiazepines (non-BZDs), 396, *398–399*
Non-injectable routes, 38
Non-narcotic antitussives, 343, *344*
Non-nucleoside reverse transcriptase inhibitors (NNRTIs), *566*, 568
Nonopioid analgesics, 385, *388–389*
Nonprescription topical medications, 219
Nonsteroidal anti-inflammatory drugs (NSAIDs), 286, 361, *362*, 385, 444–445, *447–448*, 449, 598
  misoprostol and, 304–305
Nonstimulant medications, *408–409*
Non-triptan agents, 394
Norepinephrine, *230*, 241
Norpace, 247
Nortriptyline, *391*, *414*
Norvasc, *256*
Nose drops, 53
"No substitutions," on prescriptions, 18

Nothing by mouth (NPO)
  oral administration and, 113
  rectal administration route and, 47
Novolin 70/30, 101
Novolog Mix 70/30, 101
Nucleoside reverse transcriptase inhibitors (NRTIs), *565*, 567–568
Numerator, 79
Nupercainal, 29, *208*
Nutrition facts, *191*
Nuvigil, 406
Nystatin, 211, *216*, 551, *555*

O

Occupational Safety and Health Administration (OSHA), 60
Official name, 17
Ointment, 53, *147*, *209*
Olanzapine, *427*
Olanzapine/fluoxetine, 418
Older adults
  cumulative effects of drugs, 593
  dosages, 91
  drug development and, 595
  drug overview, 593
  drug processing and, 32
  drugs that may cause mental impairment, 597
  drugs to avoid with certain medical conditions, 596–598
  issues with adherence, 601
  NSAIDs, 598
  poison and, 162
  polypharmacy, 599–601
  potentially inappropriate medication use in, 596
  vitamin B_{12} supplements and, 176–177
Olmesartan, *255*
Omega-3 fatty acids, *265*
Omeprazole, *307*
Omnibus Budget Reconciliation Act (OBRA) (1990), 9
Ondansetron, *323*
Ophthalmic immunologic agent, 361
Ophthalmic lubricants, 362
Opiate agonists, 311–312
Opioid agonists, 382
Opioid analgesics, 379–383, *383–384*
Opioid-induced constipation (OIC), 382
Opioids, 379
Oral administration (PO), 109–110, 111–116, *111–113*, *115*
Oral antibiotics, 219
Oral drug forms, 45–47, *48*
Oral route, 38
Oral syringes, 60
Orexin antagonists, 398, *399*
Orphan Drug Act (1983), 9
Orphan drugs, 9
Orphenadrine, *443*
Oseltamivir, 563–564, *564*
Osmotic agents, 284, *284*
Osmotic laxatives, 317–318, *320*
Osteoporosis therapy, 449–452, *452–453*
OTC. *See* Over-the-counter (OTC) drugs
Otic (ear) medications, 372–374, *374*
Otitis media, 372, 374
Ototoxicity, 22
Overactive bladder (OAB), 289–290
Overdoses, of vitamins, 169
Overdose, symptoms of, 171
Over-the-counter (OTC) drugs, 19, 20, 213, 404
  Advisory Committee, 20
  generic equivalents, 19
  OBRA and, 9
  product information for, 6
Oxandrolone, *510*
Oxaprozin, *448*
Oxazepam, *422*
Oxcarbazepine, 461, *464*
Oxybutynin, *236*, 290, *293*
Oxycodone, 21
Oxygen therapy, 329
Oxymetazoline, *349*
Oxytocin, 524–525, *529*

P

Pacemaker, 244
Pacerone, *250*
Package inserts, 98
Pain, dermal patch for management of, 53
Paliperidone, *427*
Palliative effects, 574

Pantoprazole, *307*
Paradoxical, 39
Paradoxical effect, 592
Parathyroid hormone, 451, *452*
Parenteral, 37, 45
Parenteral administration
  ear medications, 148–149, *148*
  eye medications, 146–147, *147*
  inhalation therapy, 128
  injections, 131–144, *132*, *137*, *138*, *139–144*
  metered dose inhaler, 128, *128*, 129
  nitroglycerin ointment, 126, *127*
  overview, 125
  routes, 37, 38
  skin medications, 146
  small-volume nebulizer home cleaning, *128*
  sublingual and buccal, 125
  sublingual or buccal administration, 125
  transcutaneous, 126–127
  use of inhaler or nebulizer, 129
Parkinson's disease (PD), 465, *465*
Paroxetine, *415*
Paroxysmal supraventricular tachycardia (PSVT), 244
Partial seizures, 458, 460
Patient counselling, calcium, 187
Patient education
  about medication, 2–3
  acne agents, 221
  acyclovir, 563
  administrations of medicine and, 98, 99
  alpha agonists, 367
  aminoglycosides, 540–541
  analgesics, 399
  androgen therapy, 510
  antacids, 302
  antiarrhythmics, 249
  antibacterial agent, 215
  antibiotics, 559
  anticoagulant therapy, *270*
  anticonvulsants, *464*
  antidiarrheal drugs, 311
  antifungals, 212
  antifungal therapy, 551
  antihypertensives, 257
  anti-infectives, 359
  anti-inflammatory ophthalmic drugs, 363
  antilipemic therapy, 266
  antineoplastic drugs, 586
  antioxidants, 192
  antiparkinsonian drugs, 471
  antipruritics, 205
  antipsychotic medications, 429
  antiretrovirals, 567
  antithyroid medication, 487
  antituberculosis agents, 554
  antitussives, 344
  beta-adrenergic blockers, 367
  beta-blockers, 232
  bismuth subsalicylate, 311
  bisphosphonates, 450
  bladder antispasmodics, 291
  bronchodilators, 336
  burn medications, 218
  calcium, 187
  carbonic anhydrase inhibitors, 365
  cephalosporins, 541–542
  cholinergic blockers, 237
  cholinergic drugs, 234
  CNS stimulants, 407
  coronary vasodilators, 259–260
  corticosteroids, 483
  decongestants, 348
  dietary supplements, 199
  digoxin, 243
  disulfiram, 432
  dosage preparation, 74
  first-generation antihistamines, 346
  food labels, 191
  generic *vs.* trade name products, 19
  hypnotics, 399
  inhaled corticosteroids, 340
  insect allergies, 161
  iron supplements, 189
  keratolytics, 207
  local ophthalmic anesthetics, 372
  loop diuretics, 282
  macrolides, 544
  miotics, 366
  mydriatics, 371
  niacin, 179
  nitrofurantoin, 561

  NSAIDs, 449, 599
  oral contraceptives, 520
  osmotic agents, 284
  pediculicides, 211
  penicillins, 545
  poisons, 163
  potassium, 185
  potassium-sparing diuretics, 283
  prostaglandin analogs, 368
  quinolones, 548
  respiratory system drugs, 350
  saline laxatives, 317
  scabicides, 211
  second-generation antihistamines, 347
  sedatives, 399
  shingles, 213
  skeletal muscle relaxants, 444
  stimulant laxatives, 318
  stool softeners, 316
  sulfonamides, 560
  tetracyclines, 549
  thiazides, 281
  thyroid medication, 485
  topical medications, 222
  type 1 and type 2 diabetes, 501
  ulcer therapy, 306
  uricosuric agents, 287
  vitamin C, 180
  vitamins and minerals, 190
Patient, for administration, 104
Patient identification bracelet, 112, *112*
Patient information interviews, 241
Patient Safety Organization (PSO), 100
Pediatric considerations, 602–604
Pediatric dosage, 89–90
Pediculicides, 210, *211*
Pegloticase, 288, *289*
PEG tube, 110
PEGylated uric acid specific enzymes, 288–289, *289*
Pellagra, 178
Penciclovir, *217*
Penicillins, 34, 544–545, *547*
Penicillin VK, *547*
Peppermint, 199
Percentages, 81
Percocet, 21, *21*
Percutaneous coronary intervention (PCI), 271
Percutaneous endoscopic gastrostomy (PEG) tube, 110, 118–120, *118*
Periods, avoidance of, 65
Peripherally acting mu-opioid receptor antagonists, 319
Peripheral saline lock (PRN adaptor), 49
Peripheral vascular disease, 271
Peripheral vasodilator, 253–254, 255, *256*
Permethrin, 210, *216*
Pernicious anemia, 176
Perphenazine, *426*
Persantine, 271, *274*
Pharmaceutical representatives, establishing rapport with, 11
Pharmacist, establishing rapport with, 11
Pharmacogenomics, 35–36
Pharmacokinetics, 29
Pharmacologic therapy, 431–432
Pharmacology, defined, 15
Pharmacology timeline, 4
pH, drug absorption and, 31
Phenazopyridine, 292–293, *293*
Phenelzine, *415*
Phenobarbital, 87
Phenothiazines, *426*
Phenylephrine, *349*, *371*
Phenytoin, 113, 245, 247, 272, *463*
Phosphodiesterase (PDE) inhibitor, 295, 510–511
Photosensitivity, 22
Physical dependence, 39
Physicians' Desk Reference (PDR), 23, 44, 89, 98
Physiological change, 29
Phytonadione, 173–174, 181
The Pill Book, 23
Pill crusher/pill cutter, 57, *57*
Pilocarpine, 56, *234*
Pilocarpine gel, *369*
Pioglitazone, 500
Piperacillin-tazobactam, *547*
Piroxicam, *448*
Pituitary hormones, 479–480, *479*
Placebo effect, 33, 379
Placental barrier, 31
Plant alkaloids, 577–578

Plantar wart, *207*
Plants, as source of drugs, *28*
Platelet inhibitors, 270–271, *274*
Platelet inhibitor therapy, 270–271
Plavix, *274*
Plunger, of syringe, 131, *132*
Poison Control Centers, 157, 158, 163
  emergency services, 158
Poisoning
  definition of poison, 157
  by ingestion, 158–159
  by inhalation, 159–160
  overview, 157
  people at risk for, 161–163
  of skin or eyes, 160
  stings and snakebites, 160–161
Polymixin B, *217*
Polypharmacy, 599–601, *599*
Port, 49
Postcoital contraception, 522, 523
Post menopausal osteoporosis, 452
Postoperative nausea and vomiting (PONV), 322
Postural hypotension, 251
Potassium, 184–185, 190
Potassium-sparing diuretics, 282–283, *284*
Potentially inappropriate medications (PIMs), 596
Potentiation, 34
Povidone–iodine, *217*
Powder, 47
PPD (purified protein derivative) skin test, 51
Pradaxa, *270*
Pramipexole, *470*
Prasugrel, *274*
Pravachol, *265*
Pravastatin, *265*
Prazosin, 255, *256*
Prednisolone, *362*
Prednisone, *482*
Prefilled cartridges, 135, *135*
Prefilled syringes, 57, 134–135
Prefilled unit-dose syringe, *78*
Pregabalin, *392*
Pregnancy, drug categories, 39
Prehypertension, 250–251
Prescription blanks/pads, 68, *68*
Prescription drug abuse, 432–433
Prescription drugs, generic equivalents, 19
Prescriptions
  legibility and, *68*
  what drugs require, 3
  who is qualified to write, 3
Primary generalized seizures, 458–460
Prinivil, *255*
PRN adapter, 49
Probenecid, 34, 287, *289*
Probenecid w/colchicine, *289*
Probiotics, 312
Procainamide, 247–248, *250*
Procardia, *255*
Procardia XL, *255*
Prochlorperazine, *323*, *426*
Procrit, *274*
Prodrugs, 32
Progesterone, 515
Progestin-containing intrauterine device (IUD), 521
Progestin hormones, 219
Progestin-only contraceptives, 521
Progestins, 515–520, *517*
Prolia, 451
Proliferating cells, 574
Propafenone, 249, *250*
Proparacaine, *371*
Proportion, 81–82
Proportion, for dosage, 86–88
Propranolol, *232*, *254*
Propylthiouracil, 486, *488*
Prostaglandin analogs, 364, 368, *370*
Prostaglandins, 525–526, *529*
Prostigmin, *234*
Protease inhibitors (PIs), *565*, 566–567
Protectants, 206, *209*, *216*
Proton pump inhibitors (PPIs), 267, 303–304, *307*
Prototype, 17
Protriptyline, *415*
Provigil, 406
Pseudoephedrine, *349*
Psoriasis, 206, *206*
Psychedelics, 3
Psychological dependence, 39
Psychological state, drug processing and, 33
Psychomotor epilepsy, 460
Psychotropic medications, 403

  alcohol, 429–432
  antidepressants, 409–414, *414–416*
  antimanic agents, 416–417, *417–418*
  antipsychotic medications/major tranquilizers, 422–427, *426–427*
  anxiolytics, 418–421, *421–422*
  CNS stimulants, 404–407
  illegal drug abuse, 433–437
  overview, 38
  prescription drug abuse, 432–433
  selective norepinephrine reuptake inhibitor, 407
  substance abuse, 429
  summary of, *428*
Psyllium, *320*
Pulmonary embolism (PE), 268, 272
Pure Food and Drug Act (1906), 5
Purified protein derivative (PPD) test, 51
Pyrazinamide, *555*
Pyrethrins, 210, *216*
Pyridostigmine, *234*
Pyridoxine, 175, 182

Q

Quality of drug, 5
Quazepam, *398*
Questran, 262, *265*
Questran Light, *265*
Quetiapine, *427*
Quinidine, *28*, 243, 246–248
Quinolones, 547–548, *554–555*

R

Rabeprazole, *307*
Racemic drugs, 413
Racepinephrine, *335*
Radioactive isotopes, 585
Raloxifene, 451, *452*
Raltegravir, *566*
Ramelteon, 397–398, *399*
Ramipril, *255*
Ranitidine, 247
Rasagiline, 468, *471*
Ratio, 81–82
Ratio, for dosage, 86–88
Recombinant DNA technology, 27
Recommended Adult Immunization Schedule, *539*
Recommended Dietary Allowances (RDA), 168–170
Reconstitution, of drug, 47
Recordkeeping, drug, 11
Rectal administration, 110, 116, *117*
Rectal drug forms, 47
Rectal medication, 116
Rectal suppositories, 53, *54*
Refills, 68
Relenza, 563
Remeron, 414
Repaglinide, *500*
Reporting medication errors, 100
Reproductive system drugs
  androgens, 508–509, *509–510*
  choice of contraceptives, 520–523, *523*
  contraceptive agents, 517–519
  erectile dysfunction medications, 510–511, *511–512*
  estrogens, 512–515
  gonadotropic hormones, 507–508
  for labor and delivery, 524–528, *529*
  other gonadotropic drugs, 529–530, *530*
  overview, 507
  progestins, 515–520, *517*
Rescue inhaler use, 332
Rescue treatment, 332
Resistance, 535–536
Respiratory depression, 397
Respiratory diseases and disorders, 328–329
Respiratory stimulants, 329
Respiratory system drugs
  antitussives, 342–343, *344*
  asthma prophylaxis, 338–339, *340*
  bronchodilators, 330–334, *334–335*
  corticosteroids, 336–337, *337–338*
  expectorants, 340–341, *341–342*
  mucolytics, 340–341, *341–342*
  oxygen, 329
  stimulants, 329
Restless legs syndrome (RLS), agents for, 472
Retavase, *274*
Retention enema, 116
Reteplase, 272, 274
Retinal, 170–171
Retinoids, 170

Retinol, 170–171, *180*
Rho kinase inhibitors, 369
Ribavirin, 564
Riboflavin, 175, *181*
Rifampin, 243, 245, 247, *555*
Rilpivirine, *566*
Rimegepant (Nurtec), 394
Risedronate, 450, *452*
Risperidone, *427*
Rivaroxaban, 268, *269*
Rivastigmine, *474*
Rizatriptan, *394*
Robitussin DM, 19
Rohypnol, 437
Romosozumab, *453*
Ropinirole, *470*
Rosiglitazone, *500*
Rosiglitazone/metformin, *500*
Rosuvastatin, *265*
Rotigotine, *471*
Route of delivery. *See* Delivery routes
Rozerem, 397
r-PA, *274*
Rythmol, 249, *250*
Rythmol SR, *250*

S

Saccharomyces boulardii, 314
Safety devices, for drug administration, 60
Safinamide, *471*
Salicylates, 309, *314*, 385–386, 444
Salicylic acid, *209*, *220*
Saline laxatives, 317, *320*
Salmeterol, *334*
Santyl, 207
Saw palmetto, 199
Saxagliptin, *500*
Scabicides, 209–210, *211*, *216*
Scabies, 209–210, *211*
Scopolamine, 126, *236*, *323*
Scored tablets, *48*, 57
Scurvy, 179
Seborrheic dermatitis, 206, *206*
Second-generation anticonvulsants, 463, *464*
Second generation antihistamines, 346–347, 349
Sedatives, 47, *398–399*
Seizures, 458
  absence, 460, 462–463
  febrile, 460, 462
  focal, 458, 460
  partial, 458, 460
  primary generalized, 458–460
  tonic-clonic, 458–459
  unilateral, 460
Selective distribution, 32
Selective estrogen receptor modifiers (SERMs), 451
Selective norepinephrine reuptake inhibitors (SNRIs), 407, 410, 413, *415*
Selective serotonin reuptake inhibitors (SSRIs), 410, 412–413, *415*, 461
Selegiline, *415*, 468, *471*
Senna, *320*
Sentinel events, 99
Septra, *28*
Serotonin norepinephrine reuptake inhibitors (SNRIs), 390
Serotonin receptor agonists (SRAs), 392–393
Serotonin-receptor antagonists, 322–323
Sertraline, *415*
Seven Rights of Medication Administration, 101–102, 104
SGLT2 inhibitor therapy, 498–499, *500*
Shaft, of needle, 132
Shingles, 213
Side effects, 22, 39–41
Signal transduction inhibitors, 583
Sildenafil, *511*
Silodosin, *296*
Silvadene, 217
Silver sulfadiazine, 217, *220*
Simethicone, *314*
Simvastatin, 34, 261, 264, 265
Sitagliptin, *500*
Sitagliptin/metformin, *500*
Skeletal muscle relaxants, 441–442, *443*
Skin, external poisoning of, 160
Skin medications (topical), 146
  acne medications, 219, *220*
  administration, 146
  antibacterial agents, 214, *214*, *217*
  antifungals, 212–213, *213*

  antipruritics, 204–205, *205*, *208–209*
  antiseptics, 215, *217*
  antivirals, 213, *214*, *217*
  burn medications, 217–219, *218*, *220*
  cautions for, 221
  corticosteroids, 205–206, *206*, *209*
  emollients, 206, *209*
  enzyme preparations, 207–208, *209*
  keratolytics, 207, *208*, *209*
  local anti-infectives, 211–215, *216–217*
  pediculicides, 210, *211*
  protectants, 206, *209*, *216*
  scabicides, 209–210, *211*, *216*
Slo-Niacin, *265*
Small-volume nebulizers (SVNs), 56, 128, *128*, 331, *331*
Smoking-cessation aids, 350–352, *352–353*
Smoking deterrent, 53
Snakebites, *160*
Soaks, 146
Sodium, 184, 190
Solid measurement, 69
Solifenacin, *293*
Solu-Medrol, 40
Solutions, 146
  aqueous, 47
  douche, 54
  injectable, 47
  oral, 47
  viscous, 47
Sources of drugs, *28*
Spina bifida, 177
Spironolactone, 282, *284*
Spironolactone and hydrochlorothiazide, *284*
Sprays, 56
Stand-alone routes, 38
Standard syringe, 132
Statins, 261–262, *265*
Status epilepticus, 460
ST-elevation myocardial infarction (STEMI), 268
Stimulant laxatives, 317, *320*
Stings, 160, 161
Stool softeners, 315–316
Streptomycin, *555*
Stroke, 266, 268, *269*
Subcutaneous (subcu) injections, 50, 132, *138*, *139*
Subcutaneous (subcu) route, 37
Subjective, 378
Sublingual (SL) administration, 125
Sublingual (SL) route, 37
Sublingual tablets, 54
Substance abuse, 429
Sucralfate, 305, *307*
Sulfamethoxazole, *562*
Sulfamylon, *220*
Sulfasalazine, 309, *314*
Sulfonamides, 560, *562*
Sulfonylureas, 495–496, *499*
Sulfur, *209*, *220*
Sulindac, *448*
Sumatriptan, *394*
Sun protection factor (SPF), 218
Sunscreens, 218–219
Superinfection, 536
"Supplement Facts" panel, 194
Supplements
  dietary, 193, 194–195
  fraudulent products, 195
  herbal and other, 193
  indications for, 169
  patient education on, 199
  quality products, 195–196
  reading and reporting, 196
Supplies, drug administration, 56–60, *57–58*
Suppository
  rectal, 47, 117–118, *117*, *118*
  vaginal, 53, *54*
Supraventricular arrhythmias, 249
Suspension
  injectable, 47
  oral, 47
Sustained-release capsule/tablet, 46, *48*
Suvorexant, *399*
Sympathomimetics, 331, *334*
Syncope/falls, 597–598
Synergism, 34
Synthetic drugs, 27, *28*
Syringes
  to administer liquid medication, 115
  parts of, 131
  prefilled, 57
  types of, 132, 133, *133*, *134*, 135, *135*

Syrup, 47
Systemic effects, 29, 125
Systemic estrogen, 219
Systems of measurement, 69–73

T

Tablets, 45, *48*
  buccal, 54
  sublingual, 54
Tachycardia, 243, 244, 253
Tadalafil, *296*, *511*
Tagamet, 246
Tall Man Lettering, 20
Tamiflu, 563
Tamoxifen, 37
Tamsulosin, *232*, 295, *296*
Tapentadol, *384*
Tardive dyskinesia, 422
Targeted therapies, 583
Tasimelteon, *399*
Taxanes, 578
Tegretol, 461
Telephone order (TO), 68
Telmisartan, *255*
Temazepam, *398*
Temovate, *209*
Temporal lobe seizures, 460
Tenecteplase, *274*
Tenofovir/emtricitabine, *565*
Tenormin, *254*
Teratogenic effect, 39
Terazosin, 295, *296*
Terbinafine, *216*
Terbutaline, 527–528, *529*
Teriparatide, 451, *452*
Testosterone, 508, *510*
Tetracaine, *371*
Tetracycline, 31, 34, 549, *555*
Tetrahydrocannabinol (THC), 435
Theophylline, 231, *335*
Therapeutic dose, 35
Therapeutic lifestyle changes (TLC), 261
Therapeutic range, 32
Thiamine, 174–175, *181*
Thiazide diuretics, 251, *256*
Thiazides, 280, *284*
Thiazolidinediones, 498, *500*
Thioridazine, *426*
Thrombin inhibitor, *270*
Thrombolytic agents, 272, *274*
Thyroid agents, 483–485, *488*
Thyroid disorders
  antithyroid agents, *488*
  thyroid agents, 483–485
Thyroid-stimulating hormone (TSH), 479, 483, 484
Thyroid (T3 & T4), 483, *488*
Thyroid, USP, *28*
Thyroxine (T4), 483
Tiazac, 46
Ticagrelor, *274*
Tigecycline, *555*
Time, for administration, 102
Tinnitus, 385
Tiotropium, *335*
Tip, of needle/syringe, 132
Tizanidine, *443*
TNKase, *274*
TNK-tPA, *274*
Tobramycin, *546*
Tocopherol, 172–173, 181
Tolbutamide, *499*
Tolerance, 39, 380
Tolnaftate, *216*
Tolterodine, 290, *293*
Tonic-clonic seizures, 458–459
Topical administration/drug forms, *52*
Topical antibiotics, 219
Topical skin medications. *See* Skin medications (topical)
Topiramate, *464*
Toprol XL, *254*
Torsemide, 281, *284*
Tourette's syndrome, 253
Toxic dose, 35
Toxic Exposure Surveillance System, 158
Toxicity, 32, 174
tPA, *274*
Trade name, 18, 19
  number as part of, 19
Tramadol, 382–383, *384*
Trandolapril, *255*

Transcutaneous (transdermal), drug delivery system, 126–127, *127*
Transdermal patch, 52, 53
Transdermal route, 37
Transderm-Scop patch, 126
Transient ischemic attacks (TIAs), 271
Tranylcypromine, *415*
Travoprost, 368, *370*
Trazodone, *416*
Tretinoin, *220*
Triamcinolone, *338*, *482*
Triamterene, 19, 282, *284*
Triamterene and hydrochlorothiazide, *284*
Triazolam, *398*
TriCor, 263, *265*
Tricyclic antidepressants, 389
Tricyclics, 410–411
Trifluoperazine, *426*
Triglycerides, 261
Trihexyphenidyl, *471*
Triiodothyronine (T3), 483
Trileptal, 461
Trilipix, *265*
Trimethoprim, *562*
Troche, 46
Tuberculin (TB) skin tests (PPD), 51
Tuberculin (TB) syringe, 133, *134*
Turmeric, 199
Tylenol, 386
Tylenol No. 2, 19
Tylenol No. 3, 19
Tylenol No. 4, 19
Tylenol poisoning, 159
Type 1 diabetes, *489*
Type 2 diabetes, *489*

U

Ubrogepant (Ubrelvy), 394
Uloric, 288
Ultraviolet (UV) radiation, 219
Umeclidinium, *335*
Umeclidinium vilanterol, *335*
Unfractionated heparin (UFH), 268, *270*
Unilateral seizures, 460
Unit-dose capsules, *78*
Unit-dose form, 77, 112
Unit-dose oral medications, *78*
Unit-dose vials, 58
United States Adopted Name (USAN) Council, 17
United States Pharmacopeia/Dispensing Information (USP/DI), 98
United States Pharmacopeia (USP), 5, 100
Units, conversion of, 72
Unstable angina, 268, 271
Urecholine, 291
Uricosuric agents, 287, *289*
Urinary analgesics, 292–293
Urinary anti-infectives, 561, *562*
Urinary system drugs
  analgesics, 292–293
  antispasmodics, 290
  benign prostatic hypertrophy (BPH) treatment, 294–295, *294*
  bladder antispasmodics, 289–290
  cholinergics, 291–292
  diuretics, 279–283, *284*, *285*
  for gout, 285–288, *286*
Urinary tract infections (UTIs), 292, *292*
U.S. Recommended Dietary Allowances (U.S. RDAs), 168
"Usual Dosage," as drug heading, 22, 23

V

Vaccines, 24, 537–538, 584–585
Vaginal creams, 53
Vaginal suppositories, 53, *54*
Valacyclovir, *564*
Valerian, 199
Valium, 113
Valproate, *417*
Valproic acid, 462, *463*
Valsartan, 255, *256*
Vancomycin, 557, *559*
Vancomycin-resistant enterococci (VRE), agents for, 557–558, *558*
Vardenafil, *512*
Varenicline, 352, *353*
Variables, affecting efficacy of drugs, 33–39
Vascular death, 271
Vascular headaches, 253
Vasotec, 255, *256*

Vastus lateralis site, 140–142, *143*
Venlafaxine, *391*, *415*
Ventricular arrhythmias, 244, 247, 249
Ventricular tachycardia, 248
Ventrogluteal site, 140, *141*
Verapamil, 243, 246, *255*, *256*, *259*
Verbal order (VO), 65
Versed, 84
Very low-density lipoproteins (VLDLs), 261
Vials, 57–58
Vibramycin, 18
Viscous solutions, 47
Vitamins
  antioxidant, 192
  fat-soluble, 169, 170–174, *180–182*
  folic acid, 177, 182
  indications for supplements, 169
  megadoses of, 169
  niacin, 178, 182
  vitamin A, 170–171, 180
  vitamin B$_1$, 174–175, *181*
  vitamin B$_2$, 175, *181*
  vitamin B$_6$, 175, *182*
  vitamin B$_{12}$, 176–177, 182
  vitamin C, 178–179, 182, 192
  vitamin D, 171–172, 181, 186
  vitamin E, 173, 181
  vitamin K, 173–174, *181*
  water-soluble, 169, 174–182
Vomiting, poisoning and, 158
Vortioxetine, *415*
Vytorin, *265*

W

Wakefulness-promoting agents, 406–407
Warfarin, 37, 174, 266–267
  vitamin K and, 174
Warning labels, 6, *30*
Water-soluble vitamins, 174–182
Web sites, as source of drug information, 24
Weight, drug processing and, 33
WelChol, 262, *265*
www.cdc.gov/vaccines, 24
www.fda.gov, 24
www.ismp.org, *66*, 67, *67*
www.nlm.nih.gov/medlineplus, 24
www.pharmacist.com, 24
www.safemedication.com, 24
www.usp.org, 24

X

Xalatan, 368
Xanthine oxidase inhibitors, 288, *289*
Xanthines, 333–334, *335*
Xarelto, 267, *269*
X-ray dyes, allergic reactions to, 40
Xylocaine, *250*

Y

Yetley, Elizabeth, 196
Yohimbe, 195

Z

Zafirlukast, *340*
Zaleplon, *399*
Zanamivir, 563, *564*
Zestril, *255*
Zetia, 264, *265*
Zileuton, *340*
Zinc, 189, 191
Zinc insulin vials, rotating, *502*
Zinc oxide, *209*
Zinc oxide ointment, *28*
Ziprasidone, *427*
Zocor, 34, 261, *265*
Zoledronic acid, *453*
Zolmitriptan, *395*
Zolpidem, *398*
Zovirax, 213
Z-track injection method, 144, *144*
Zyloprim, 288